出國報告(出國類別：開會)

2024亞太肝病聯盟肝細胞癌政策論壇
2024 Hepatocellular Carcinoma (HCC) APAC Policy Forum
報告

服務機關：衛生福利部國民健康署

姓名職稱：魏璽倫副署長

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派赴國家/地區：泰國曼谷

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報告日期：113 年 12 月 24 日

摘要

2024亞太肝病聯盟肝細胞癌政策論壇 (2024 Hepatocellular Carcinoma (HCC) APAC Policy Forum) 於10月初在泰國曼谷舉行，聚焦於亞太地區肝細胞癌監測與管理議題，探討肝細胞癌監測與管理的最佳實例、關鍵政策建議及可行的行動方案，以促進亞太地區各國於肝細胞癌防治上的實質變革，並分享日本的肝細胞癌監測的策略模式，作為其他亞太地區實施的參考。

本署以國家政策制定者的角色，參與論壇之專題討論 (panel discussion)，並於工作坊 (workshop) 中與醫療專業人士、公共衛生學者、數據分析專家及病友團體等各利益關係者協作，草擬出臺灣肝細胞癌監測管理計畫路線圖；藉由參與此次論壇的機會，增進瞭解亞太地區肝細胞癌監測做法，並與國際專家討論交流、分享臺灣致力於肝病防治之成果。

目次

壹、　目的

2024 亞太肝病聯盟肝細胞癌政策論壇係由亞太肝病聯盟 (APAC Liver Disease Alliance) 主辦，泰國公共衛生部醫療服務司、泰國國家癌症研究所、日本肝臟學會合辦。

肝細胞癌是肝癌的主要類型，為亞太地區第 5 大常見的癌症，同時也是亞太地區第 2 致命的癌症類型。僅於 2020 年當年，亞太地區即有 61 萬新肝細胞癌發生病例，占全球發生率的 73%；全球肝細胞癌死亡病例有 72%發生在亞太地區，達 56.6 萬人。值得注意的是，肝細胞癌的病人有 80%在晚期才被診斷出來，這對治療結果具有負面影響，不利於患者預後。

因此，本次論壇邀請各國分享有關肝細胞癌早期偵測和及時治療的策略，以改善患者的治療效果；聯合政策制定者、醫療專業人士、病友團體和專家，共同於專題討論中探討肝細胞癌相關防治策略，以提高對風險因子及早期偵測需求的認識，同時促進各界合作與政策發展；工作坊則以國家別作為分組，組員為自己的國家建立有效的國家肝細胞癌監測管理計畫路線圖。

藉由此次參加論壇的專題討論交流，更瞭解亞太地區肝細胞癌監測管理的做法，並分享臺灣致力於肝病之成果，促進各界對亞太地區肝病防治的合作。

貳、 過程

亞太肝病聯盟成立於2023年1月，是亞太地區第一個致力於解決肝硬化、肝細胞癌和病毒性肝炎等肝病的平台。其主要目標為促進肝病預防、早期發現、及時轉診，以及促進研究，做為公私對話的平台，並強調有效肝病預防、控制和管理的重要性。該聯盟於2023年7月與Vista Health共同發布了「消除亞洲的無聲緊急狀況：肝炎和肝細胞癌(Eliminating Asia’s Silent Emergency: Hepatitis and Hepatocellular Carcinoma)」白皮書（如附件1），目的在於評估亞太地區肝病的現況、調查各地區的差異，以日本監測模型作為黃金標準 (gold standard)，並基於實證提供適合亞太地區之國家肝炎行動計畫和國家肝細胞癌監測計畫的藍圖。

亞太肝病聯盟以上述白皮書為基礎辦理此次論壇，將論壇規劃為3個主要部分：第1部分包括開幕致詞 (opening address)、主題演講 (keynote) 和專題演講 (lecture)，由駐曼谷美國大使館疾病管制中心及泰國公共衛生部政府官員、來自日本的專家和臨床醫師等進行分享，此部分重點在於說明日本肝細胞癌監測和管理之成功經驗，以及日本如何成為監測與管理肝細胞癌的典範；第2部分進行專題討論 (panel discussion)，內容涵蓋亞太地區肝細胞癌監測與管理的現狀，探討最佳實踐與現存方式差異之處，並思考未來可行的方向，以改善肝細胞癌患者的治療歷程。第3階段為2小時的工作坊 (workshop)，依國家別進行分組討論，由組員共同制定出更完善有效的國家肝細胞癌監測管理計畫路線圖。會後亞太肝病聯盟將以此次論壇的內容為依據，發表一份政策報告作為公私合作工具和指導方針，期幫助推動亞太地區肝病的革新。

此次論壇議程如下：

時段	流程	主題	講者
上午 9:00-9:10	歡迎詞	開場 解決亞太地區肝細胞癌問題：多利益相關者和多邊方法	Roberta Sarno女士 亞太肝病聯盟主任
上午 9:10-9:20	主題演講1	在公共衛生中優先考慮肝細胞癌：泰國公共衛生部的見解	Sakarn Bunnag醫師 醫療服務司副司長 泰國公共衛生部
上午 9:20-9:30	開幕致詞	開幕致詞	Christine Ross醫師 疾病管制中心駐泰主任 駐曼谷美國大使館
上午 9:30-9:40	主題演講2	日本消除肝細胞癌的策略：日本肝臟學會的政策觀點	考藤達哉 (Tatsuya Kanto) 教授 肝炎免疫研究中心主任

			日本國立國際醫療研究中心 日本肝臟學會
上午 9:40-9:50	專題演講1	亞太地區肝細胞癌的流行病學、臨床和經濟負擔：緊急呼籲加強認同、國家計畫和病友旅程觀點	Will Brown先生 資深總監 Vista Health
上午 9:50-10:10	專題演講2	臨床醫師觀點：以日本肝細胞癌管理為領先模式	工藤正俊 (Masatoshi Kudo) 教授 胃腸病學和肝病學系教授兼系主任 日本近畿大學醫學部 日本肝臟學會
上午10:10-10:20中場休息			
上午 10:20-10:30	專題演講3	衛生部的觀點：日本的肝病防治措施	清野宗一郎 (Soichiro Kiyono) 肝炎預防與控制辦公室助理主任 日本厚生勞動省
上午 10:30-10:40	專題演講4	優化肝細胞癌監測： PIVKA-II、演算法和強化患者治療與護理的臨床與經濟效益	Pisit Tangkijvanich教授醫師 肝炎和肝癌卓越中心主任 泰國Chulalongkorn大學
上午10:40-11:00中場休息			
上午 11:00-12:00	平行場次1	進度報告：亞太地區肝細胞癌監測與管理	主持人： 工藤正俊 (Masatoshi Kudo) 教授 與談人： 1. Murallitharan Munisamy博士： 馬來西亞國家癌症協會董事總經理 (Managing Director) 2. Do Thi Ngat女士： 越南衛生部醫療服務管理司官員 3. Teerha Piratvisuth教授： 泰國肝臟研究協會科學計畫主席 4. Simone Strasser教授： 澳洲皇家阿爾弗雷德王子醫院主任兼資深專員 5. Somchai Thanasitthichai醫師： 泰國公共衛生部國家癌症研究所所長 6. 魏璽倫博士： 臺灣衛生福利部國民健康署副署長 7. 楊雯雯女士： 臺灣病友聯盟顧問
中午12:00-下午1:00午餐			
下午1:00-1:20團體照			
下午	平行場次2	成功案例：肝細胞癌監測和管理	主持人：

1:20-2:20		的有效實踐	Roberta Sarno主任 1. 陳建仁院士： 臺灣中央研究院基因體研究中心特聘研究員 2. Jacob George教授： 澳洲Westmead醫院胃腸肝病科主任 3. 考藤達哉 (Tatsuya Kanto) 教授： 日本肝臟學會、日本國立國際醫療研究中心肝炎免疫研究中心主任 4. Dorothy Keefe教授： 澳洲癌症協會執行長 5. Norlen Bin Mohamed博士： 馬來西亞衛生部疾病控制組非傳染性疾病科科長 6. Luckxawan Pimsawadi博士： 泰國肝癌病友小組負責人 7. 蒲若芳博士： 臺灣輔仁大學數據科學中心執行長 8. Poowanai Sarkhampee博士： 泰國Sunpasitthiprasong醫院肝胰膽外科和移植科高級專業級別醫師
下午 2:20-4:20	工作坊	共同制定亞太地區強健的國家肝癌監測管理計畫路線圖	Will Brown先生 資深總監 Vista Health
下午4:20-4:40中場休息			
下午 4:40-4:50	閉幕	結語：反思與未來方向	Roberta Sarno女士 亞太肝病聯盟主任

各講者簡報及各國分組討論所產出之國家肝細胞癌監測管理計畫路線圖如附件2，論壇之各部分重點摘錄如下：

一、 第1部分：主題演講及專題演講

(一)主題演講

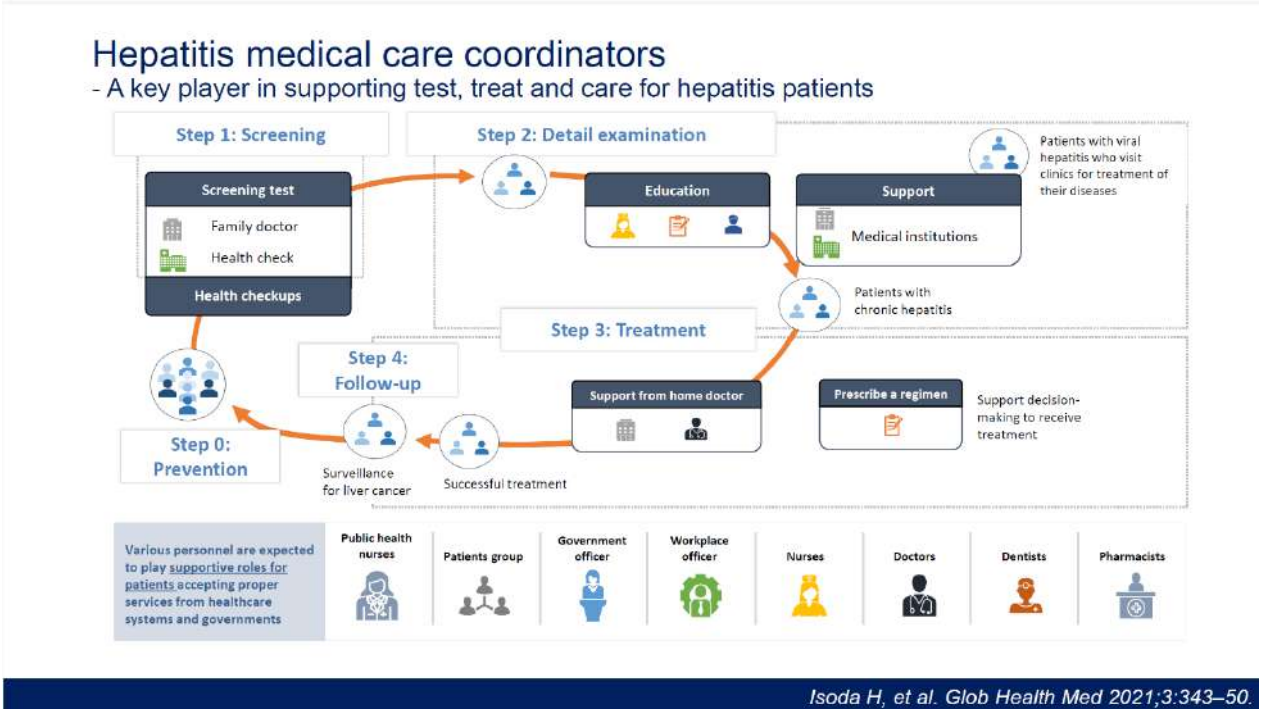
肝細胞癌是肝癌的主要類型，為亞太地區第5大常見的癌症、第2致命的癌症類型。僅在2020年，亞太地區有61萬新肝細胞癌病例，占全球發生率的73%；全球72%的肝細胞癌死亡病例發生在亞太地區，達56.6萬人。特別值得注意的是，80%的肝細胞癌病例在晚期被

診斷出來，這對治療結果具負面影響，不利於患者預後。分析亞太地區幾個關鍵的成功因素，包括：具國家層級的肝細胞癌監測計畫、充足的政治意願與協調能力、持續且充足的資金支持來推行國家計畫、具健全的監測、教育及精確高品質治療。

與其他亞太地區相似，肝細胞癌亦是泰國癌症死亡主因，是泰國男性中最常見的癌症、泰國女性中第3常見的癌症，每年約有2萬名新病例和1萬6千名死亡病例，且通常在晚期才被診斷出來，治療選擇亦受限。過去的20年中，泰國肝癌發生率和死亡率已持續下降，可能與公眾疾病意識的提升、B型肝炎疫苗的接種、提供B、C型肝炎的篩檢，以及增強服務和轉介系統有關。其中發生率下降最重要的因素，乃因1992年開始逐年擴大實施新生兒B型肝炎疫苗接種計畫，而成功使年輕世代的B型肝炎感染率顯著下降。目前主要針對35至55歲群眾（此群人為疫苗施打政策之前出生的族群）進行B型肝炎和C型肝炎篩檢。此外，過去泰國治療B、C型肝炎皆由專科醫師主責，為增加治療的可近性，目前泰國已制定全科別醫師 (general practitioner) 治療B型肝炎和C型肝炎之指引，並辦理相關培訓計畫，將治療擴大至全科別醫師處理。

觀察日本的長期趨勢，肝細胞癌死亡率於1970年到2002年間逐漸增加，近年來則呈現下降趨勢，主因為B、C型肝炎所導致的肝癌死亡減少，然而酗酒相關的肝癌在日本則顯著增加，非酒精性脂肪性肝炎 (Nonalcoholic steatohepatitis, NASH) 導致的肝癌死亡率也有上升的趨勢。總體來說，隨著政府全面地管理病毒性肝炎，日本的整體肝癌死亡率呈現下降的趨勢。日本的B、C型肝炎病毒帶原人數，2015年較2000年減少了大約100萬人。此外，日本的診斷率和治療率遠高於全球平均。目前日本的挑戰在於仍有部分未被診斷的感染者，甚至仍有約40萬名已確診為陽性者尚未納入治療和照護體系。

日本於2009年頒布「肝炎對策基本法 (Basic Act on Hepatitis Measures)」，推動病毒性肝炎患者的全面防治措施，包括篩檢、治療及照護。民眾可以享有終身一次免費的肝炎篩檢，如果檢測結果呈陽性，可以免費接受包括超音波檢查在內的深入檢查，以確定是否需要進一步治療。對於需要治療的患者，可利用醫療保險和補助計畫降低昂貴的醫療費用，另也有為肝癌患者及針對因肝硬化病情惡化的患者，設立特別補助計畫，支持肝癌患者重複治療的費用，以減輕患者的經濟負擔。日本肝臟學會已分別於2022年及2024年更新B型和C型肝炎臨床治療指引，旨為醫療人員提供可行的方案，以確保患者能夠獲得一致的抗病毒治療。此外，日本致力於培訓專業的健康照護工作者，稱為「肝炎醫療協調員 (Hepatitis medical care coordinators)」，他們來自不同的機構，包括公共衛生護士、



Isoda H, et al. Glob Health Med 2021;3:343–50.

患者團體、政府官員、藥劑師以及牙醫師等組成團隊，其目標為面臨不同困難和健康狀況的患者提供包括健康教育、治療指導，或是心理支持。通過這種多元化的合作模式，讓患者能夠獲得更全面的照護，從而提高治療的效果和患者的生活品質（如上圖）。

日本已建立肝癌監測系統，早期肝癌診斷比例逐年上升，肝癌死亡率亦逐步下降。日本肝臟學會積極與亞洲各國肝臟學會合作，2023 年與臺灣肝臟研究學會及韓國肝臟研究學會簽署合作備忘錄，成立「東亞肝臟聯盟」(East Asia Liver Alliance, EALA)，旨在促進彼此間的交流，共同對抗病毒性肝炎和肝臟疾病。

(二)專題演講

1.首先由Vista Health的資深總監Will Brown先生說明「消除亞洲的無聲緊急狀況：肝炎和肝細胞癌」白皮書中的重點：

有關亞太地區肝細胞癌的臨床及經濟負擔，以中國為例，每年肝細胞癌造成的經濟損失高達110億美元，如不介入處理，預計2030年時將增加至340億美元。案例研究顯示，消除肝炎可對整個地區帶來巨大的投資報酬率，並且顯示肝細胞癌的監測極具成本效益。因此，投資於消除肝炎及肝細胞癌監測，將能達到臨床和經濟上的雙重效益。白皮書提出5個政策建議，以應對亞太地區的迫切需求：(1)各國國家行動計畫應更具全面性；(2)擴大肝炎篩檢和治療並整合於現存的健康體系中，並且依照不同的場域訂定合適的方案；(3)資金問題，需要探索如何將肝炎和肝細胞癌整合，納入更廣泛的健康倡議，以使資金利用最大化；(4)實施全面的肝細胞癌監測計畫，確保患者能夠及時獲得治療；(5)提升公眾疾病意識，並促進社區由下而上的倡議，以推動整個生態系統的承諾。

2.來自日本近畿大學醫學部的工藤正俊 (Masatoshi Kudo) 教授，以一個臨床醫師的角度，來探討日本肝細胞癌的管理機制：

日本國家監測計畫於1980年啟動，肝細胞癌5年存活率，從1978至1982年的5.1%，提升到2003至2005年的42.7%，這和肝細胞癌腫瘤標記PIVKA-II、AFP-L3檢測與健康保險覆蓋、手術技術進步，包括局部消融療法、經導管動脈化學栓塞療法 (TACE) 和肝動脈灌注化學治療 (HAIC) 等有關。日本全國性資料顯示肝細胞癌患者早期（期別0+A）占67%、中期（期別B）占27%、晚期（期別C+D）僅占6%，且67%的肝細胞癌患者已接受過治癒性治療。依據全球傳染病和流行病學網絡GIDEON (Global Infectious Disease and Epidemiology Network) 橫跨5大洲、39國家、共計超過3300名來自日本、亞太地區、歐洲和北美肝細胞癌患者的資料顯示，從初次診斷到死亡的整體中位數存活 (Median overall survival) 月數，以日本（79.6個月）的表現最佳，優於歐洲（25.0個月）、亞太地區（20.9個月）、拉丁美洲（19.5個月）及美國（14.8個月），各分期的中位數存活情形亦均顯著高於其他地區。進一步分析肝細胞癌篩檢者相較於未篩檢者，在調整lead-time bias後，篩檢者存活率顯著優於未篩檢者，顯示篩檢確能提高患者接受治癒性療法的機會，並延長患者的生存期。日本肝細胞癌患者的存活率在全球名列前茅，主要歸功於國家監測計畫，能有效地早期發現肝細胞癌並及時治療。

日本肝臟學會肝細胞癌臨床實踐指引 (JSH HCC clinical practice guideline) 建議高風險及極高風險群接受篩檢；高風險群包括慢性 B、C 型肝炎感染者與肝硬化患者（但實務上，非肝硬化性的非酒精性脂肪性肝炎 (NASH)/ 代謝性脂肪肝疾病 (MAFLD) 也會納入監測)，極高風險群則為 B、C 型肝硬化患者；篩檢工具包括腹部超音波和甲種胎兒蛋白 (AFP)、AFP-L3、PIVKA-II 3 種腫瘤標記，日本的社會保險均有給付。值得注意的是，此 3 種腫瘤標記的檢測結果彼此間沒有相關性，因此日本肝臟學會建議至少使用 2 種以上的腫瘤標記來監測肝細胞癌。針對高風險群的監測措施為每 6 個月進行 1 次腹部超音波檢查及前揭 3 種腫瘤標記檢測；對於極高風險群，監測需更為頻繁，除了每 3 至 4 個月進行一次腹部超音波檢查及 3 種腫瘤標記檢測之外，另建議每 6 至 12 個月進行 1 次 dynamic CT/MRI。

治療方面，上揭肝細胞癌臨床實踐指引內亦有詳述。在日本，透過多專科團隊的合作、以病人為中心的照護模式，所有肝細胞癌患者皆能透過保險給付，輕鬆獲得高品質、先進的治療，包括切除、移植、消融、超選擇性的經導管動脈化學栓塞療法 (superselective TACE)、全身與局部療法的聯合治療 (combination of systemic and locoregional therapy) 以及合併免疫治療。

日本肝臟學會為增進大眾、肝病病友團體對肝病的疾病意識，以及強化國家監測體系中，非肝臟專科醫師及護理、健康從業人員對肝病風險分級的瞭解，於日本 47 個都道府縣辦理教育宣導；日本肝癌醫學會則自 1967 年起辦理全國肝細胞癌登記，每 2 年發布一次報告。2 個學會之間經常彼此合作，辦理相關活動，而學會及病友團體於政府政策制定的過程中，亦有進行遊說的管道。

綜上，工藤教授認為監測肝細胞癌高風險及極高風險群，能提高患者接受治癒性治療機會，進而延長患者存活，同時減少晚期肝細胞癌的醫療費用。此外，民間團體應和政府合作，積極推動全國性的肝細胞癌監測系統。

3.日本厚生勞動省肝炎預防與控制辦公室助理主任清野宗一郎 (Soichiro Kiyono)，分享日本衛生部對抗肝病的相關措施：

日本肝炎防治措施大事紀如下：

1985年：開始B型肝炎母嬰傳染預防計畫。地方政府在中央政府補助一半費用的支持下，

實施篩檢和預防措施，包括提供孕婦HBsAg檢測、提供HBsAg陽性孕婦HBeAg檢測、對HBsAg陽性和HBeAg陽性母親產下的新生兒施打B型肝炎免疫球蛋白 (HBIG) 和3劑B型肝炎疫苗。

1995年：HBIG和B型肝炎疫苗納入健康保險給付。

2006年：因B、C型肝炎集體訴訟案件，肝炎病毒感染成為社會關注議題。

2008年：啟動「肝炎綜合對策」。「C型肝炎救濟特別措施法 (Law on Special Measures against Hepatitis C)」生效（針對因纖維蛋白原產品感染者）。

2010年：「肝炎對策基本法 (Basic Law on Hepatitis Measures)」生效。

2012年：「B型肝炎救濟特別措施法 (Law on Special Measures against Hepatitis B)」生效（針對因預防接種而感染者）。

2016年：B型肝炎疫苗被納入「預防接種法 (Immunization Law)」下的常規接種清單，為所有新生兒施打B型肝炎疫苗。

2018年：開始為肝癌和重度肝硬化治療患者，依其收入狀況提供公費補助。

日本政府於2024財政年度投入肝炎防治之總預算約168億日圓，促進肝病治療約84億日圓、推動肝炎病毒檢測及重症預防約39億日圓、強化各地治療體系約5億日圓、肝炎防治正確宣導約2億日圓、相關研究經費約38億日圓。2010年實施的「肝炎對策基本法」為日本肝炎防治措施提供法源基礎，明定中央和地方政府、醫療保險機構、人民和醫師的職責，並制定推動肝炎防治措施的指導方針。指導方針是由肝炎策進委員會回饋意見給政府衛生部門，並經過相關行政單位討論、提交文件後，最終由衛生部長決定；指導方針至少每5年檢視一次，並可隨時根據需要進行更新。肝炎防治基本措施包括預防和早期偵測、肝炎醫療照護平等及研究之推動，以尊重肝炎患者的人權並消除歧視。

各個都道府縣都至少設有1家以上的指定「肝病核心醫院」，為民眾提供肝病相關資訊、收集並提供肝病專科醫療機構資訊，為醫療保健專業人員辦理培訓課程和講座、提供民眾肝病相關的諮詢和支持、與其他醫療機構建立肝病討論平台、建立可提供肝癌多專科治療的醫療系統。此外，肝炎醫療協調員在日本促進肝炎照護上，扮演了關鍵的作用，各界參與人員各運用其專業來協助肝炎防治工作，共同推廣民眾對肝炎的認識、提供諮詢和

建議，鼓勵人們接受肝炎篩檢、向患者說明肝炎支援系統，以及消除民眾對患者的偏見和歧視，透過多學科、多方位專業人員協作，來有效對抗日本的肝炎問題，減少肝硬化與肝癌的發生。另外，也運用多管道策略的全國宣傳活動，增進對肝炎的公眾疾病意識。

日本設定2030年肝病目標如下：

(1)B型肝炎：使用核酸類藥物治療之5年累積HBsAg陰性率 (Cumulative 5-year HBs-antigen-negative rate)，從2022年的3%，提升到2030年的5%；
(2)C型肝炎：慢性肝炎及代償性肝硬化 (compensated cirrhosis) 的持續病毒反應率 (Sustained virological response, SVR) 率：從2022年的95%，提升到2030年的100%；
(3)失代償性肝硬化 (Decompensated cirrhosis)：Child-Pugh B患者的2年存活率，從2022年的70%，提升到2030年的80%；Child-Pugh C患者的的2年存活率，從2022年的45%，提升到2030年的55%；
(4)肝癌：年齡標準化的罹病率，從13%降至7%；
(5)C型肝炎失代償性肝硬化持續病毒反應率：從2022年的92%，提升到2030年的95%。

總之，日本肝病防治關鍵策略包括：

(1)預防體制，包括以疫苗接種和安全血液措施，來預防B型和C型肝炎病毒的傳播；
(2)追蹤體制，包括以篩檢識別肝炎感染者、以醫學詳細檢查評估肝損傷程度、提供適當治療以遏止疾病進展及併發症；
(3)創建健全的醫療體系，為肝炎患者提供高品質的醫療服務；
(4)保護患者權利，肝炎相關的污名和歧視問題；
(5)促進研究：投資於研究以開發新的治療和預防策略，提升國人生活品質。

4.泰國Chulalongkorn大學醫學院Pisit Tangkijvanich教授分享新的監測肝細胞癌工具：

泰國2022年有18萬3,541名新發癌症個案，11萬8,829人死於癌症，肝癌新發個案2萬7,936人（占15.2%），位居癌症新發個案之首。其中非肝硬化的肝細胞癌病人中，代謝性脂肪肝病 (Metabolic dysfunction-associated steatotic liver disease, MASLD)（占38.5%）大約是B型肝炎病毒感染（占21.7%）的2倍。目前泰國欠缺完整的監測系統，難以評估肝細胞癌政策施行成效，估算僅約2.5%的病人接受治癒性治療。

國際上的指引大多建議針對高風險族群，尤其是肝硬化的病人，每6個月使用腹部超音波合併AFP進行肝細胞癌監測。但有篇統合了32個研究、包括1萬3,367病人的資料分析顯示，以腹部超音波合併AFP來偵測早期肝細胞癌，敏感度約為63%（特異度84%），但考量病人遵從度僅約24%，所以大約只能找出15%的肝細胞癌的病人。若結合其他生化指標，例如PIVKA-II (DCP)，並以GAAD score（即依性別(G)、年齡(A)、AFP(A)、DCP (D) 4個參數進行計算）評分系統來評估早期肝細胞癌，能提升敏感度（70%）及特異度（90%），且病人遵從度較高（約44%）；使用Markov model評估不同監測工具的成本效益顯示，以GAAD最具成本效益，或許可成為監測肝細胞癌的新工具。

二、第2部分：專題討論

(一)平行場次 1 主題：進度報告：亞太地區肝細胞癌監測與管理

由日本近畿大學醫學部工藤正俊教授主持，請場次 1 的成員分享他們的經驗，包括各地區或國家肝細胞癌盛行率及主要成因、現行的監測與管理情況、國家監測政策的關鍵績效指標、面臨的挑戰，以及未來如何改善監測與管理計畫。摘要如下：

1.國民健康署副署長魏璽倫博士：在臺灣，以預防勝於治療為主要政策規劃重點。早期診斷、早期治療最有經濟效益，疾病的監測系統與架構也是如此。尤其，臺灣面臨人口老化以及各種慢性病人口增加的情況下，醫療負擔與日俱增。臺灣訂有國家肝炎及肝癌防治計畫，政府透過跨部門的合作，結合衛生教育宣導、肝炎及肝癌篩檢、健康保險、癌症登記及死因通報等資料，來建置肝細胞癌監測系統，定期分析數據，並成立「衛生福利部肝癌及肝炎防治會」以及「B、C 型肝炎防治辦公室」，持續監測肝炎與肝癌的變化情況，並定期召開會議，諮詢肝病相關醫療專家與公共衛生專家，透過多面向討論，積極找出肝病防治對策。整體而言，臺灣的醫療資源充足，政府也鼓勵醫療人員主動協助民眾早期偵測肝病，以更有效益的模式進行肝細胞癌的治療與管理。政府針對肝癌的預防與控制採取多元策略，從 2011 年至 2021 年，早期肝癌患者接受根除性治療的比例，從 76%提升至 89%，這是我國肝癌的重要品質指標，目前我們也持續密切監測這一指標。此外，肝炎的盛行率、診斷與治療率、肝癌的發生率、診斷時的分期分布、存活率和死亡率，都是臺灣政府評估肝癌監測政策效能的關鍵績效指標。肝細胞癌治療主要是由全民健康保險給付，在臺灣，全民健康保險覆蓋率達 99%，以及醫院提供一致性的癌症治療品質，也大大提升民眾接受癌症治療的意願。健保制度中，對於手術、用藥是否納入保險給付項目等，有完整的討論與決定機制。因醫療發展快速日新月異，然而醫療資源有限，是否納入疾病治療

方式的給付項目，其中難免會有競爭，也必須有所取捨，中央健康保險署正積極利用醫療科技評估 (health technology assessment, HTA) 制度，以確保病人的治療需求。

2.馬來西亞國家癌症協會董事總經理 (Managing Director) Murallitharan Munisamy 博士：在馬來西亞，導致肝細胞癌的原因正逐漸轉變，以往是病毒性肝炎，現在非傳染性因素的比例逐漸增加。政府開始注重上游的預防管理，即非僅針對肝細胞癌本身進行治療，而是積極針對肝炎進行預防和管理，刻正推動大量 B 型和 C 型肝炎的社區外展篩檢和教育工作。我們當前主要專注的核心方向是納入對非病毒性肝細胞癌致病因子的篩檢。另外在治療方面，我們與埃及和藥品專利池 (Medicines Patent Pool) 合作，推出了我們自己的等效治療方案，並加強與印度的合作，引進了其他針對性治療的學名藥。這使得治療 C 型肝炎的費用變得可負擔。此外，馬來西亞山區的地方，近年我們與新加坡合作發展行動醫療車，卡車上有醫師、護士和技術人員等，能提供即時檢測及腹部超音波等，但某些方面的資源分配與使用仍面臨挑戰，免疫療法的可及性亦更具挑戰性。我們已經與製藥公司建立良好合作關係，針對特定免疫療法訂定支付計畫，努力改善免疫療法的可獲得性，從而降低患者的經濟負擔。

3.澳洲皇家阿爾弗雷德王子醫院 Simone Strasser 教授：在澳洲，肝細胞癌的病因在過去 20 年中具顯著的變化，與 B 型或 C 型肝炎有關的肝細胞癌比例持續下降。澳洲與 B 型肝炎有關的肝細胞癌，主要集中在原住民群體及移民群體，包括來自亞太地區、太平洋群島、非洲和東歐的移民，而且超過 30%的患者尚未確診。2016 年隨著引進直接作用抗病毒藥物 (DAAs)，大部分 C 型肝炎患者已接受治療，但仍有大約 7 萬名患者未治療。NAFLD/MAFLD 所導致的肝細胞癌負擔日增，且有許多患者在沒有肝硬化的情況下，便已發展出 NAFLD/MAFLD。肥胖、糖尿病以及酒精的使用，已成為肝細胞癌重要的風險因子，因此，如何及早識別這些高風險患者，成為澳洲目前最大的挑戰，下一步則是實施有效的監測計畫。目前正在執行大規模的教育計畫，該計畫旨在針對基層醫療領域的從業人員進行教育，幫助他們識別有代謝疾病風險因子的肝病患者，以便這些患者能夠進入肝細胞癌的監測計畫。澳洲目前的監測，主要仍依賴腹部超音波和 AFP 檢測，且醫院尚未獲得 PIVKA-II 的經費支持。公立醫院系統內進行腹部超音波檢查是免費的，但如果是在私人機構，則有可能免費、也可能部分醫院會向患者收取部分的額外費用，若患者無法或不願支付這筆費用，則可能因而選擇不進行檢查；另外，在澳洲某些地區，例如偏遠原住民社區的腹部超音波檢查可近性不足、取得高品質的腹部超音波檢查有所侷限，此外，尤其是肥胖率日益增長的人群中，肥胖會導致腹部超音波的篩檢失敗率較高。如果能以血液檢測作為篩

檢工具的替代，則執行上將更為理想。目前澳洲尚未有國家肝癌監測計畫，因此，缺乏關於肝細胞癌篩檢及早期偵測的全國性數據，這使得針對肝細胞癌的綜合管理和政策制定更加困難。但澳洲擁有完善的國家健康體系，為患者提供廣泛的治療途徑和支持，多數患者由多學科團隊管理，團隊根據患者的疾病階段以及治療可行性，依據巴塞隆納肝癌分期(BCLC) 提供最佳治療方案，並靈活調整策略；晚期或中晚期肝細胞癌患者在特定的情況下，僅需支付少量共同負擔費用。

4.泰國肝臟研究協會科學計畫主席 Teerha Piratvisuth 教授：在泰國，肝細胞癌目前最常見成因仍然是 B 型與 C 型肝炎。由於疫苗接種，20 歲以下的 B 型肝炎感染率已顯著下降，我們建議針對 35 歲民眾進行 B 型和 C 型肝炎篩檢，並且與肝炎與肝癌等相關學協會合作，教育民眾接受免費肝炎篩檢。隨著飲食西化，肥胖問題逐漸增加，因此非 B、C 型肝炎及 MAFLD，也逐漸成為泰國肝硬化和肝細胞癌的重要病因之一，約 40%的 MAFLD 患者可能會直接進展為肝癌，這是目前面臨的重要挑戰之一。另外，目前監測方法以腹部超音波為主，等待時間長，患者平均每 6 至 9 個月才能安排一次檢查，且肥胖患者的比例上升，肥胖會對腹部超音波影像判讀造成限制。而 AFP 檢查的敏感度不高，我們在十多年前的一項研究中發現，僅約 60%肝細胞癌患者中有 AFP 升高的情形，剩下的 40%為 AFP 陰性的肝細胞癌患者，且 AFP 的升高可能是由其他原因引起的，尤其是在患有 F1 期纖維化的患者中，有可能因 B 型肝炎惡化或肝臟發炎，而出現 AFP 升高的現象。影響肝細胞癌監測還有一個最主要的障礙，是全科醫師缺乏相關的認知，雖然他們可能知道哪些是高風險患者，但他們認為這些患者應該交由專家或專科醫師處理，而導致他們未主動進行監測。此外，治療 B 肝需要民眾醫囑遵從度高，因為 B 肝病毒持續久，希望未來有能發展出對抗 B 型肝炎新藥。前面專題演講有提到的 GAAD score，是我們正在努力推動作為監測肝細胞癌的新工具。至於泰國政府治療政策，患者若需接受最新療法（如免疫療法），通常需要自費，除非有特定批准且詳細說明治療的必要性，目前的健康保險僅涵蓋有限的療法，主要集中在成本效益較高的選擇。

5.越南衛生部醫療服務管理司官員 Do Thi Ngat 女士：肝細胞癌是越南最常見的癌症之一，也是癌症死亡的主要原因，然而在監測方面，我們尚未擁有全面的數據。目前政府已意識到這問題的嚴重性，並正更新相關指引，致力於強化肝細胞癌的預防和管理策略。我們的國家級醫療體系和設施集中在城市地區和幾個主要大型醫院。因此，如何在基層醫療層級的醫院和醫師之間推動，是未來需要解決的問題之一。越南目前也僅有少數免疫治療藥物列入治療清單，使用仍有限制。

6.泰國公共衛生部國家癌症研究所所長 Somchai Thanasitthichai 醫師：泰國公共衛生部專注於 B 型與 C 型肝炎病毒控制，並採用疫苗接種和抗病毒療法等措施，來降低肝細胞癌的發生，未來將強化對高風險族群進行早期偵測，以改善肝細胞癌患者的存活。泰國國家癌症研究所已與其他學術機構合作，發布肝細胞癌管理的指導方針，提出以下措施：(1)擴大抗病毒治療的覆蓋面：為 B 型和 C 型肝炎患者提供更多治療機會，允許全科醫生開立治療處方，不限專科醫師；(2)推動早期肝細胞癌的外科手術和介入技術的應用。另外，建議針對高風險族群進行監測，包括每 6 至 12 個月進行 AFP 檢測及其他相關檢查。但目前國內面臨篩檢資源不足、後續診斷及治療階段的資源的匱乏，也可能影響肝細胞癌管理的全面落實。我們正持續推動多項宣傳活動，以提高大眾對肝細胞癌的疾病意識，強調早期診斷的重要性，並鼓勵接受治療。此外，也加強培訓醫療提供者辨識肝細胞癌的徵兆與症狀，以及如何指導患者進行早期偵測。泰國自 2017 年開始，肝細胞癌發生率已逐漸下降，早期肝細胞癌從之前 10%也已增加至 30%，但目前多數患者在確診時已屬於晚期，因此如何提高診斷早期肝細胞癌的比率，仍然是一個重大挑戰。

7.臺灣病友聯盟顧問楊雯雯女士：肝細胞癌篩檢所需的腹部超音波、AFP 和 PIVKA-II，都已納入全民健康保險覆蓋範圍。然而，PIVKA-II 檢測僅限於高風險患者，並受到嚴格的標準限制。篩檢監測方面，目前因為篩檢由不同的機構及部門負責，因此篩檢監測數據分散於多個資料庫，可能導致某些疑似陽性患者未及時被追蹤，進而延誤治療。我們希望政府能建立一套機制，以促進數據整合。臺灣擁有健全的全民健康保險，因此我們能夠提供抗病毒藥物 DAAs 治療 C 型肝炎。此外，我們也已推行 B 型肝炎疫苗的全國性新生兒接種計畫。基於這些基礎，如果能投入更多資源，我認為臺灣在早期治療肝細胞癌方面，具有良好的條件。我們建議政府尋找多種資金來源例如：產業捐款、環境污染費用或酒精稅收；強化推廣資通訊（ICT）及數位醫療技術，以縮小城鄉差距，提供遠距醫療服務，減少患者因就醫需長途奔波的時間與資源浪費，實現資源分配公平性。也希望政府在一些重要會議中，可以廣納我們病友團體或患者的意見，讓患者不僅成為政策的觀察者，更成為積極的參與者。

(二)平行場次2主題：成功案例：肝細胞癌監測和管理的有效實踐

由亞太肝病聯盟主任 Roberta Sarno 主持，請場次 2 的成員分享來自不同國家的肝細胞癌監測與管理的實例，包含成功的最佳實踐、目前存在的缺口和需要關注的領域，以及未來需要努力的方向。摘要如下：

1.澳洲 Westmead 醫院胃腸肝病科主任 Jacob George 教授：澳洲擁有全民健康系統，為肝癌患者提供免費治療。澳洲目前正實施第 6 版國家 C 型肝炎計畫，此計畫將持續到 2030 年，我們很有可能會成為全球第 1 或第 2 個消除 C 型肝炎的國家。針對 B 型肝炎，我們有第 4 版國家 B 型肝炎計畫，內容涵括所有相關利害關係者，並且定有明確的目標，此外，我們也訂定了 MAFLD 相關指引，去年也發表了「肝癌控制路徑圖」，並發布肝癌指引。澳洲面臨的一大挑戰是國土廣闊。肝細胞癌監測的執行能力，從大都市到偏遠地區逐漸減弱，偏遠地區實務上無法完全按照指引進行。大都市的醫學中心，肝細胞癌的監測與照護非常出色，然而基層醫療面臨醫療人力不足，使得肝細胞癌監測的難度增加，加上偏遠地區腹部超音波檢查的取得非常有限，且治療效果通常與患者的社經地位和健康識能息息相關等因素，以致偏遠地區肝細胞癌治療效果較大都市地區差。此外，澳洲面臨的挑戰與其他國家有所不同，多數 C 型肝炎感染與注射毒品有關、B 型肝炎好發於移民群體，因此相關議題較難獲得政治人物的重視。

2.澳洲癌症協會執行長 Dorothy Keefe 教授：澳洲 2023 年啟動了國家癌症行動計畫，這個計畫是基於結果的平等，而非資源的平等，這表示必須將資源放在需要的地方，而且不僅是針對肝細胞癌，每一位癌症患者都一樣重要。其中一個實務應用是建立一個國家級導航框架及綜合性癌症網絡，每一位患者，無論他們身處於澳洲的哪一個角落，都能獲得所需的照護。我們的雄心壯志是儘可能地將照護提供在離患者住家最近的地方，並且整個過程能夠無縫的進行運作。目前還無法存在真正的無縫對接，但我們現階段的目標，是將偏遠地區與市中心無縫連接。我們的主要城市中有多個綜合癌症中心，作為綜合性癌症網絡的樞紐，職責為與所負責區域內的每一個機構建立聯繫，並涵蓋全國各角落。此外，我們正開發一個癌症數據框架，使分散的數據能夠全國共享，並利用這些數據來確認是否實現癌症計畫中的目標及各種癌症的最佳照護，包括肝細胞癌的照護。肝細胞癌雖然只是澳洲第 12 常見的癌症，但它卻是第 6 大致死原因，需要進行成本效益分析，也需要有一個清晰的計畫，來確定未來的運作模式。

3.中央研究院基因體研究中心陳建仁院士：臺灣很早就開始進行肝癌監測計畫，肝癌在 1980 年代初期為臺灣死因之首，因此 1984 年臺灣領先全世界開始實施新生兒 B 型肝炎疫苗接種，至今 40 歲以下的臺灣人皆已受惠，然而 40 歲以上的感染者仍需要關注。2003 年開始推行 B 型和 C 型肝炎的抗病毒治療，符合資格可獲得免費治療，我們也定期檢討放寬這些治療標準，納入更多人接受抗病毒治療。我們對 45 至 79 歲的民眾進行篩檢，全面進行 B 型和 C 型肝炎檢測，目前約有 57%的人已完成檢測。我對於臺灣能在 2025 年消除 C

型肝炎非常有信心，但消除 B 型肝炎情況則相對困難，因為在臺灣盛行率約 15%到 20%，在亞洲是最高的國家之一，我們目前仍在努力尋求如何讓更多患者接受抗病毒治療。B 型和 C 型肝炎的感染者，會被轉介至健保醫療服務，接受定期的照護，包括腹部超音波檢查和 AFP 檢測的監測，對於晚期肝癌患者，可以接受免疫療法和標靶治療，但由於預算限制，目前僅允許患者接受 1 次免疫療法，這方面我們需加強，需爭取更多的資源以提供更完整的治療選擇。我們也應敦促製藥公司降低費用。例如，在我們的 C 型肝炎治療計畫中，與製藥公司進行很好的談判，這使得臺灣能夠推出全國性 C 型肝炎消除計畫。努力降低成本，這將是我們的另一個策略。至於肝細胞癌早期檢測，目前使用腹部超音波和 AFP，但尚未有全國性的 PIVKA-II 檢測，目前待評估其成本效益，並將其作為針對高風險人群監測的策略之一；與脂肪性肝病有關的疾病，我們需要決定是否進行一般人口篩檢，還是只針對高風險群體進行篩檢。必須將患者分為不同的風險群體來實施篩檢，這一點對於改善篩檢的效果至關重要。此外，我們也面臨城鄉差距的問題，需要被重視並加強，以協助偏遠地區建立完善的肝癌篩檢和監測系統。

4.臺灣輔仁大學數據科學中心執行長蒲若芳博士：臺灣對於肝癌防治的努力可以追溯到很早期，就已經推行國家層級的疫苗接種計畫，但我認為當時這項政策的制定過程中，並沒有進行足夠的成本效益分析。後來有一些專家試圖進行成本效益的估算，藉此幫助我們瞭解這類公共衛生政策如何造福臺灣民眾以及整體社會。我認為，這種思考方式或相關分析工作是非常值得進行的。臺灣在全民健保開始實施後，政府和專家都非常努力地試圖將所有的治療指引落實到位，但健保支付與否的決策中，成本效益分析成為其中一個重要的部分，幫助指引政策方向並確保資源的合理分配。政策制定時，我們不僅要考慮其影響，還要評估其對民眾和政府的價值。不僅僅是預算上的考量，還包括如何讓資金發揮最大的價值，這在確保資源永續利用時尤其重要。如果臺灣要做得更好，首先，要有更精準的工具或方法，能夠幫助我們識別高風險族群。此外，目前的系統似乎對於那些沒有回診的患者，缺乏更積極的關注，當然這部分也涉及到患者的責任和義務，但我認為現在是進行思維轉變的時候，也許應該納入更多的工具和演算法來幫助識別高風險族群，也許可以運用應用程式或護理人員，提醒高風險族群應該做什麼、但卻還沒有去執行，讓這個計畫能夠觸及那些真正需要的人。另一個仍需改善的地方，是臺灣在肝癌晚期治療方面的效果並不理想，這是目前的現況，或許許多國家也面臨相似的挑戰，因為我們正面對許多高成本、昂貴的藥物，同時醫療系統也承受著巨大的壓力。在資源有限的情況下，新的技術、新的藥物、新的設備不斷湧現，這對決策者來說是一個挑戰，或許我們的政府應該更專注於這

些領域，理解這是長期的投資，因此，我們也應該思考如何改善財務運作，以減輕全民健保或政府方面的壓力。

5.泰國 Sunpasitthiprasong 醫院肝胰膽外科和移植科 Poowanai Sarkhampee 醫師：肝細胞癌在泰國很常見。我們醫院的肝細胞癌患者中，有 71%的病例因腫瘤擴散或其他因素而無法手術。約有 7、8 成的病人無法提供治癒性治療，是泰國最主要的問題。我希望患者不要罹患疾病，預防是對患者最好的方式。但如果患者已罹患疾病，我們希望是早期的病例，因為早期階段，我們能為患者提供治癒性治療，例如手術、移植或其他相關操作。作為外科醫生的觀點，要幫助患者做好準備，從患者旅程的早期到最後一步，以滿足他們的期望。我認為泰國的醫療保健系統也應該主動與雇主溝通，讓他們更了解如何幫助篩檢陽性的員工申請工作以及如何繼續下去。也期望政府能繼續促進所有風險族群的肝細胞癌篩檢活動和早期診斷，擴大全國各地的臨床管道，以便能獲得某些藥物，以及那些最有效、最實惠的全面醫療服務。

6.泰國肝癌病友小組負責人 Luckxawan Pimsawadi 博士：我代表肝癌病友團體分享泰國的觀點。病友與家屬缺乏知識去認識早期症狀，也缺乏判斷接受何種治療方式，然而，這對於無法取得合適治療的患者很重要。我認為同儕倡議者 (peer-to-peer advocacy) 策略，能有效率地協助泰國肝細胞癌患者，患者能夠諮商志願者，例如醫師、護士或存活者等，或是志願者透過肝炎、肝癌社群網站，分享最佳治療選擇，並告知患者如何獲得潛在醫院的治療，這在泰國的偏遠地區尤為重要。分享的資訊也包含疾病旅程、如何申請保險給付，以減輕病友準備文件遭遇的困難。

7.馬來西亞衛生部疾病控制組非傳染性疾病科科長 Norlen Bin Mohamed 博士：監測癌症是一件重要的事，馬來西亞的癌症登記已有 15 年以上的歷史，肝癌在馬來西亞癌症的發生排名，由第 8 名升至第 5 名，使得醫療負擔加劇。目前國家癌症防治計畫正在審閱程序，因此現在應是納入肝細胞癌監測的好時機，刻正由肝細胞癌專業團隊策畫中。目前已納入的是 B、C 型肝炎強制篩檢，希望未來可以監測肝細胞癌。目前我們的挑戰也包括脂肪肝、肥胖盛行率增加，因此我們需訂定標準的指引，來正確處理現況。對政策制定者而言，成本效益也很重要。

8.日本肝臟學會、日本國立國際醫療研究中心肝炎免疫研究中心主任考藤達哉 (Tatsuya Kanto) 教授：我認為日本成功的關鍵在於監測計畫運行良好，可以及時發現早期的肝細胞癌患者，而且這些患者可接受適切治療、達到治癒效果。首先，要能篩檢出病毒性肝炎

患者，然後針對高風險群進行進一步篩檢，此為發現早期肝癌並能夠進行治癒性治療的關鍵行動。當然，資金問題也至關重要，包括特別補助計畫及全面的醫療保險制度，還有針對抗病毒治療、癌症治療和失代償性肝硬化治療的特別補助計畫，減輕民眾負擔。日本肝癌主要仍與病毒性肝炎相關，但與其他國家類似，非病毒引起的肝癌病例也持續增加，因此面臨的挑戰在於如何找出 MAFLD 患者中的高風險人群。目前日本尚未有針對此高風險人群的篩檢策略，因此，需考慮並建立某種篩檢流程來覆蓋這群人。

三、第3部分：工作坊

與會者依國籍分組，包括澳洲、印度、南韓、馬來西亞、臺灣、泰國、越南等7個衛生系統的與會者，臺灣分組成員有陳建仁院士、高雄長庚紀念醫院盧勝男醫師、臺大醫院蘇東弘醫師、蒲若芳執行長、楊雯雯顧問、台灣年輕病友協會劉桓睿副理事長以及本署，並由Vista Health的Colin Tan先生引導討論，成員依自己不同的觀點集思廣益，透過各利益關係者協作，就患者旅程階段（疾病意識、預防、早期偵測、診斷及治療）所遇到的問題，討論肝細胞癌監測和管理的最佳實踐方式，並由Colin Tan先生整理出臺灣的肝細胞癌防治路線圖（詳見附件2會議資料）。

(一)疾病意識：高風險的族群對於常見的風險因素可能不夠熟悉，臺灣有「我的健康存摺」應用程式，記載包括個人的健康數據、疾病診斷、藥物和病史，我們討論出來的共識，是希望未來能夠透過此應用程式，提供更加個人化的健康教育訊息，告訴患者應該做什麼，而非不應該做什麼，並為主要群體建立及生成風險預測模型，如此一來可以針對高風險患者進行篩檢以減輕國家經費的負擔，因為國家並沒有足夠的預算為所有人進行篩檢。我們希望跨部門能共享數據，政府衛生部門也與勞動部門積極合作，正在努力說服公司或雇主上傳員工的健康檢查數據，而這些數據的收集回饋，有助於找到高風險群體。

(二)疾病預防：國民健康署與中央健康保險署合作推動「全民健康保險代謝症候群防治計畫」，建議透過相關計畫，讓代謝症候群的民眾也意識到罹患肝細胞癌的風險。其實對於民眾直接宣導「健康」概念，效果可能不顯著，現在社交軟體上運動風氣盛行，或許可以運用民眾社交心理及愛美的天性，來推廣身體活動或進行相關的健身運動。或是結合保險公司已有的一些附加保險，推出一些患者或一般民眾若參加健身房或進行更多運動，可以對應降低保險費的方案。

(三)早期偵測及診斷：我們提供腹部超音波、AFP的費用，但PIVKA-II僅限於部分患者，

如果可以定義出高風險患者，並為更多患者進行早期偵測及診斷，或許對於後續的治療能更有效益。

(四)疾病治療：關於治療的可及性，與其他國家的做法類似，目前免疫療法僅限於部分符合條件的患者。病友團體期望參與健保或健康政策的制定，因為他們是接受治療的人，他們希望發聲、為更多的肝細胞癌患者的治療爭取相關補助。

參、　心得及建議

這次藉由參與2024亞太肝病聯盟肝細胞癌政策論壇，深入了解亞太地區各國在肝細胞癌監測與管理上的現況、挑戰與機會。論壇不僅匯集了各國的政策制定者、醫療專業人士、研究學者和病友團體，更透過專題演講、專題討論和工作坊等形式，激盪出許多寶貴的觀點和可行的策略。下一步，亞太肝病聯盟也將啟動整合此次各國的做法為政策文件，並邀請參與者共同撰寫及發表一份政策報告，作為公私合作的工具和指導方針。

一、肝細胞癌除了患者所承受的身體痛苦外，還帶來了國家龐大的經濟負擔。將本次論壇中亞太各國所提共同面臨的困難，整理如下：

(一)肝細胞癌是亞太地區的嚴峻挑戰：肝細胞癌是亞太地區重要的公共衛生議題，不僅是第5大常見癌症，同時也是第2大致命的癌症。2020年亞太地區新增的肝細胞癌病例占全球的73%，死亡人數則占全球的72%。這些數據凸顯了肝細胞癌在亞太地區的嚴峻性，亟需各國政府與社會各界共同關注與努力。

(二)肝細胞癌晚期診斷是主要問題：值得注意的是，約有80%的肝細胞癌患者在晚期才被診斷出來， 這對治療結果產生負面影響，不利於患者的預後。這顯示早期偵測的重要性，以及各國現有監測體系仍有待加強之處。如何更有效率地篩檢出早期肝癌患者，是各國共同的目標。

(三)肝細胞癌病因轉變：過去肝細胞癌主要與B型和C型肝炎病毒感染有關，但近年來，部分國家非酒精性脂肪性肝炎（NASH）和代謝性脂肪肝疾病（MAFLD）等非傳染性因素所導致的肝細胞癌比例逐漸增加。這代表除了持續關注病毒性肝炎外，也需將代謝性疾病納入防治重點。

(四)資源限制： 許多國家在肝細胞癌的監測和治療資源上仍有限制。例如，某些國家缺乏完善的監測系統，尚需建立或整合數據；或是在偏遠地區難以取得高品質的超音波檢查。此外，免疫療法等較新的治療方式，在部分國家仍未普及，且費用高昂。這些資源限制使得肝細胞癌的防治工作更具挑戰性，如何更有效地利用資源是關鍵。

二、從日本的成功經驗所得到的啟示：日本的肝細胞癌防治策略是多面向且全面的，從預防到治療，從政府到民間團體，都積極參與其中。以全國性的監測計畫為基礎，提供全面性的肝炎防治措施，結合完善的醫療體系和多方合作模式，致力於早期發現、及時治療，

並減輕患者負擔。

(一)國家級監測計畫：日本自1980 年即啟動國家監測計畫以來，早期肝癌診斷比例逐年上升，肝細胞癌5年存活率亦顯著提升、死亡率逐步下降。其成功的關鍵在於針對高風險群進行篩檢、早期偵測和及時治療。除了腹部超音波之外，聯合使用多個腫瘤標記，提高篩檢的準確性。

(二)全面性的肝炎防治措施：日本於2009年頒布、2010年實施「肝炎對策基本法」，推動病毒性肝炎患者的全面防治措施，包括篩檢、治療及照護，並且持續更新B型和C型肝炎臨床治療指引。民眾可享有終身一次免費的肝炎篩檢，若檢測結果呈陽性，可免費接受深入檢查。對於需要治療的患者，則有醫療保險和補助計畫來降低醫療費用。日本政府為此投入大量的經費，2024財政年度投入肝炎防治總預算約168億日圓。而這些措施為日本的肝細胞癌防治的前端，奠定了堅實的基礎。

(三)健全的醫療體系：透過多專科團隊的合作、以病人為中心的照護模式，所有肝細胞癌患者皆能透過保險給付以及補助計畫，獲得高品質、低負擔的先進治療，包括切除、移植、消融、超選擇性經導管動脈化學栓塞療法、全身與局部療法的聯合治療以及合併免疫治療等多種治療方式。各都道府縣亦皆至少設有1家以上的指定「肝病核心醫院」，提供肝病相關資訊、諮詢和支持。

(四)多方協作模式：日本除了政府的投入外，肝臟學會、醫療機構、病友團體和肝炎醫療協調員等也扮演重要角色。肝炎醫療協調員來自不同機構，提供健康教育、治療指導和心理支持，確保患者能獲得全面的照護。日本肝臟學會與肝癌醫學會經常合作，辦理相關活動，並參與政府政策制定。這種多元化的合作模式，值得其他國家學習。

(五)日本仍面臨一些挑戰：本次主辦單位以日本在肝細胞癌防治的監測模型作為黃金標準(gold standard)，即使如此，目前存在有部分未被診斷的肝炎感染者，甚至有已確診但尚未納入治療體系的患者；酗酒相關的肝癌和NASH導致的肝癌死亡率有上升趨勢。如何找出代謝性疾病患者中的高風險人群，目前尚未建立合適的篩檢策略。

三、臺灣現況及未來建議

臺灣慢性肝病及肝硬化標準化死亡率已經從87年的每10萬人口23.2人，降至112年的每10萬人口9.5人，降幅達59.1%；肝癌的標準化發生率已由93年最高點的每10萬人口40.7

人，降至111年的每10萬人口23.7人，降幅達41.8%；肝癌標準化死亡率則由85年最高點的每10萬人口29.5人，降至112年的每10萬人口16.4人，降幅達44.4%，顯見臺灣的肝病防治策略，已顯見成效。然而肝癌死亡率仍排名癌症死亡的第2名。

亞太肝病聯盟2023年7月發布「消除亞洲的無聲緊急狀況：肝炎和肝細胞癌(Eliminating Asia’s Silent Emergency: Hepatitis and Hepatocellular Carcinoma)」白皮書中提到，消除肝炎及肝細胞癌的4個關鍵因素包括：制定國家計畫、足夠的政治意願及協調、充足的資金、消除/控制工作的執行。在B型肝炎的4項評比，僅臺灣和做為黃金標準的日本，4項目皆得到綠燈；在C型肝炎的4項評比，僅臺灣、澳洲和做為黃金標準的日本，4項目皆得到綠燈；然而，在肝細胞癌的4項評比，僅有做為黃金標準的日本4項目皆得到綠燈，臺灣則皆為黃燈，各項目未達標分析原因如下：

(一)制定國家計畫：我國國家癌症防治計畫中未包含肝癌，且我國宣導之五癌篩檢亦不包括肝癌，以致國際評比可能認為我國未有肝癌之國家級計畫或篩檢策略。事實上，臺灣已有「國家肝炎及肝癌防治計畫」，本署亦提供成人健檢，先找出HBsAg或anti-HCV陽性之高危險群，結合中央健康保險署執行之B型肝炎帶原者及C型肝炎感染者醫療給付改善方案，即為現有之國家級肝癌監測計畫。

(二)足夠的政治意願及協調：原因同上。事實上，我國「衛生福利部肝癌及肝炎防治會」每半年定期召開會議，持續監測肝炎與肝癌的變化情況，諮詢肝病相關醫療專家與公共衛生專家，透過多面向討論，積極找出肝病防治對策。

(三)充足的資金：肝細胞癌早期檢測，目前使用腹部超音波和AFP腫瘤標記，而PIVKA-II檢測之健保給付適應症需為肝硬化之慢性肝炎且符合有限的條件，與做為黃金標準的日本相較起來，腫瘤標記檢測種類及對象涵蓋範圍較為不足。

(四)肝癌控制工作的執行：日本肝臟學會定有肝細胞癌臨床實踐指引，且供全國作為一致性的準則，我國醫療院所目前則依據中央健康保險署肝癌篩檢及治療相關項目的支付範圍及B型肝炎帶原者及C型肝炎感染者醫療給付改善方案來執行。

新一期「國家肝炎及肝癌防治計畫」(2026-2030) 刻正修訂中，未來建議可銜接現行兩署已有之作為並納入計畫中，至於是否參考日本的經驗，訂定臨床實踐指引、納入至少3種腫瘤標記檢測種類、擴大高風險群體的定義、放寬給付規定，待相關主責機關進一步

評估及規劃。日本持續性和系統性的肝細胞癌防治策略，其成功經驗值得亞太國家借鑒，但同時也要考慮各國的獨特性，制定因地制宜的策略。這次論壇提供了一個寶貴的平台，讓各國能分享經驗、交流觀點、共同為亞太地區的肝細胞癌防治而努力。我國過去在肝炎防治的表現成果斐然，相信在肝細胞癌的防治上，持續強化早期偵測、加強公眾疾病意識、建立整合性照護體系、促進跨部門合作、支持研究與創新，並重視防治資源運用的永續性，臺灣肝細胞癌防治工作在國際上肯定能大放異彩，作為各國的典範。

肆、　論壇照片

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<tr><td>以國家政策制定者的角色參與論壇之專題討論</td><td>與本次論壇主辦單位亞太肝病聯盟主任 Roberta Sarno 女士交流</td></tr>
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<tr><td>Colin Tan 先生於工作坊中引導來自臺灣的成員協作草擬臺灣肝細胞癌監測管理計畫路線圖</td><td>來自臺灣的人員與亞太肝病聯盟主任 Roberta Sarno 女士合照</td></tr>
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APAC Liver Disease Alliance

ELIMINATING ASIA'S SILENT EMERGENCY:

HEPATITIS AND HEPATOCELLULAR CARCINOMA

White Paper Prepared by Vista Health
July 2023

vista health

About the APAC Liver Disease Alliance

The Alliance was launched in January 2023 and consists of founding members including diagnostics companies such as Abbott and Roche, as well as academia, NGOs, liver coalitions, patient groups, and experts. The APAC Liver Disease Alliance is the first platform in the Asia-Pacific region dedicated to addressing a wide range of liver diseases, including cirrhosis, hepatocellular carcinoma, and viral hepatitis. Its primary goals are to promote prevention, early detection, timely referral, and research in the field of liver diseases. This Alliance serves as a neutral platform for public-private dialogues, emphasizing the importance of effective liver disease prevention, control, and management while advocating for optimal policies that benefit both health systems and society as a whole.

To find out more about or get involved with the APAC Liver Disease Alliance, please visit https://apacliverdiseasealliance.org/.

Co-authors
We would also like to thank the following representatives from the strategic partners of the APAC Liver Disease Alliance for co-authoring this White Paper:

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01 Foreword

Ms Capucine Pénicaud
Director, Program and Partnership, The Hepatitis Fund

The release of the first APAC Liver Disease Alliance White Paper is timely. It addresses the clear need for better linkage between hepatitis care and cancer care in the APAC region, where liver diseases contribute to significant mortality, economic losses, and grief in communities from this region. Hepatitis deaths in Asia-Pacific account for more than half of the global death toll and hepatitis is the leading cause of liver cancer.

This Paper highlights the gaps in HBV and HCV policy, funding, and screening. Importantly, it provides a strong, practical five-point plan to address gaps in the hepatitis and liver cancer landscapes across APAC. At the Hepatitis Fund, we firmly believe that hepatitis care is cancer prevention, and we are pleased that the Alliance is actively working to fill that gap and working towards integration, both upstream towards public health approaches to infectious diseases and downstream towards cancer screening and care.

We are confident that this White Paper will pave the way for more significant collaborations and partnerships that can make a real difference in the lives of those affected by liver diseases.

Dr John Ward
Director, Coalition for Global Hepatitis Elimination

In an era characterized by advances in medical science and public health, an unyielding health crisis remains: viral hepatitis and its complications such as hepatocellular carcinoma. These present a significant socio-economic burden in the APAC region, where hepatitis deaths have accounted for 63% of the global death toll.

In response to this pressing issue, the APAC Liver Disease Alliance has released its first White Paper for hepatitis and HCC. Central to this White Paper is a pragmatic five-point action plan that represents a blueprint to encourage funding allocation and guide the implementation of national hepatitis action plans and national HCC surveillance programs, tailored to the Asia Pacific context.

As a diverse alliance focused on Asia Pacific, the APAC Liver Disease Alliance is uniquely positioned to support the outlined policy recommendations, and its work will play a pivotal role in implementing strategies that enable more robust linkages between public health approaches to infectious diseases and downstream HCC surveillance and care.

We at the Coalition for Global Hepatitis Elimination are committed to working together to expand access to HBV and HCV services and improve early detection of HCC. It is our sincere hope that this White Paper serves not just as a guiding document, but as an ignitor of further collaborations and partnerships to accelerate progress towards HBV and HCV elimination in APAC.

02 Executive Summary

Liver diseases, which can be caused by viral infections, inherited conditions, obesity and alcohol misuse, have a significant impact on public health in the Asia-Pacific (APAC) region, where 63% of global deaths from liver diseases occur. Without systemic action, this public health emergency threatens to worsen. This paper focuses specifically on hepatitis and liver cancer, also known interchangeably as HCC (hepatocellular carcinoma) given that it is the most common type of liver cancer. While non-alcoholic steatohepatitis (NASH) and non-alcoholic fatty liver disease (NAFLD) contribute to HCC development, viral hepatitis, particularly HBV and HCV, remains the primary cause of HCC in APAC.

The aim of this white paper is to assess the current landscape of liver diseases in APAC, investigate gaps and provide evidence-based recommendations to reduce the clinical, economic, societal, and humanistic burden of hepatitis and HCC and improve public health in the APAC region.

ECONOMIC AND CLINICAL BURDEN OF HEPATITIS AND HCC

3 times higher
hepatitis death rate compared to HIV/AIDS

AUD 26 billion
in lost productivity due to HCV-related absenteeism, presenteeism, and premature deaths

610,000
new cases of liver cancer in APAC in 2020

72%
of total HCC deaths worldwide were attributed to APAC alone

USD 11.1 billion
estimated economic burden caused by HCC in 2019, equivalent to 0.047% of the local GDP

The current landscape for liver diseases was assessed through a targeted literature review of international and national sources, including journal publications and expert roundtable outputs. Efforts towards eliminating hepatitis need to be intensified as most APAC territories are not on track to eliminate hepatitis and reduce the burden of liver cancer by 2030, despite the World Health Organization (WHO) Global Health Sector Strategy (GHSS) on viral hepatitis setting out this target for elimination of viral hepatitis.

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2.1 CRITICAL SUCCESS FACTORS FOR HEPATITIS ELIMINATION

The presence of a national plan, sufficient political will and coordination, adequate funding, and well-established screening and treatment integrated within existing health systems and tailored to the needs of different populations in different settings are key to hepatitis elimination. The challenges and recommendations were raised, developed and refined through the collaborative efforts of leading hepatitis and HCC experts, including a Liver Alliance Charter workshop ***(the Alliance Charter can be accessed here)*** and a roundtable discussion organised by the alliance in Feb 2023.

2.2 CRITICAL SUCCESS FACTORS FOR COMPREHENSIVE HCC MANAGEMENT

We base the critical factors for effective HCC surveillance and management on Japan's gold standard surveillance model and opinions of other regional key opinion leaders in HCC. The factors identified include the presence of a national HCC surveillance program, sufficient political will and coordination, adequate funding, extensive surveillance protocols, public education, careful and accurate treatment selection, and high-quality treatment techniques. Adequate funding is crucial for the successful implementation of comprehensive HCC surveillance programs utilizing ultrasound and tumour markers.

2.3 THE INVESTMENT CASE FOR HEPATITIS AND HCC

We also present the investment case for increasing investment in hepatitis elimination and comprehensive HCC management in the region. A comprehensive HBV elimination program consisting of diagnosis, linkage to care, and treatment is cost-effective and saves health system resources. Screening for HCV can lead to significant cost savings, and combining screening with treatment will lead to a high return on investment. Biannual ultrasound and AFP (Alpha Fetoprotein) tumour marker test are the most cost-effective surveillance methods for patients with cirrhosis and chronic HBV.

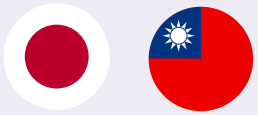
HEPATITIS ELIMINATION AND HCC SURVEILLANCE IS COST SAVING

USD 2.23 **USD 1.70**

By 2035, every USD 1 spent on HBV elimination in Philippines and Vietnam will return USD 2.23 and USD 1.70 respectively

USD 9.1 billion

net economic benefit in Pakistan by 2050 if USD1.45 billion is invested in HCV elimination



-33% **+15%**

Cost of illness (COI) trended downwards in Japan with the presence of a national surveillance program while COI trended upwards in Taiwan between 2002 and 2014

2.4 POLICY RECOMMENDATIONS FOR HEPATITIS AND HCC

Based on the evidence of the health and economic benefits associated with tackling liver diseases, there is a clear need for APAC governments and all stakeholders to take decisive action. We propose five key actions that are needed to reduce the burden of Hepatitis and HCC in the APAC region:

1. HEPATITIS NATIONAL ACTION PLANS NEED TO BE MORE COMPREHENSIVE

- → **Set clear elimination goals** and targets and actively track progress.
- → **Leverage resources** to support budget-based planning and implement localized strategies.
- → **National actions plans need to be costed and funded** under local budgets or utilize catalytic funding to kick-start
- → **Set up a national steering committee** to track progress of elimination in line with targets set

2. EXPAND HEPATITIS SCREENING AND TREATMENT, INTEGRATED WITHIN EXISTING HEALTH SYSTEMS AND TAILORED TO THE NEEDS OF AFFECTED POPULATIONS IN VARIOUS SETTINGS

- → **Adopt the recommended stepwise approach** (4-steps) to develop a national hepatitis screening strategy.
- → **Integrate hepatitis initiatives** into existing health systems, broader health initiatives and infrastructure to improve linkage to care.

3. GOVERNMENTS CAN SECURE GREATER FUNDING BY INTEGRATING HEPATITIS AND HCC INTO BROADER HEALTH INITIATIVES AND EMPLOYING BLENDED FINANCING MODELS

- → **Frame funding** as part of the universal health coverage to advocate for domestic resources.
- → **Leverage catalytic funding from global funding bodies** to kickstart programmes by implementing micro elimination strategies

4. IMPLEMENT A COMPREHENSIVE NATIONAL HCC SURVEILLANCE PROGRAM AND ENSURE TIMELY ACCESS TO TREATMENT FOR HCC AND HEPATITIS

- → **Learn from the gold standard:** a sustainably financed and thoughtfully implemented HCC surveillance program like Japan's.
- → **Amplify surveillance efforts** among high-risk populations to accelerate access to care.

5. INCREASE AWARENESS AND IDENTIFY POLICY CHAMPIONS TO DRIVE POLITICAL COMMITMENT

- → **Launch public awareness activities** to promote health equity and combat stigma.
- → **Secure buy-in and mobilize support** from policy champions and seize policy windows to generate momentum for action.

In conclusion, there is an urgent need to address liver diseases in APAC, which are causing the death of approximately 1.5 million people every year in the region. Every stakeholder in the ecosystem, from policymakers and funders to physicians and patients, has something to offer and gain. The APAC Liver Alliance aims to unite all stakeholders to tackle the rising liver disease epidemic in the region. Investing in these diseases offers a positive return on investment and the opportunity to reduce suffering and death for millions every year.

03 Introduction

3.1 LIVER DISEASES POSE A SIGNIFICANT THREAT TO PUBLIC HEALTH IN ASIA-PACIFIC

The Asia-Pacific (APAC) region is home to 60% of the world's population and accounts for 63% of global deaths due to liver diseases[1]. Cirrhosis, liver cancer, and acute viral hepatitis are the top three contributors to liver-related deaths in the region, with cirrhosis being the leading cause[1]. HBV and HCV caused 67% of cirrhosis-related deaths and 60% of liver cancer deaths in APAC[1].

While all hepatitis viruses can cause acute hepatitis, a short term inflammation of the liver, only Hepatitis B (HBV), Hepatitis C (HCV) and Hepatitis D (HDV) frequently cause chronic hepatitis, a condition marked by ongoing liver inflammation lasting more than six months[2]. Left untreated, chronic hepatitis can lead to severe complications, including liver cirrhosis and hepatocellular carcinoma (HCC).

HCC is the most common type of liver cancer in APAC and along with hepatitis, imposes a significant economic burden. In countries like Thailand with a high HCV prevalence, incorporating sofosbuvir-based regimens to treat HCV infection poses a significant financial burden to the Thai Universal Healthcare Coverage. Simply getting from a 10% to 30% treatment coverage under this regimen would require a budget increase to 150% and 450% respectively[3]. This underscores the costly nature of HCV, with the average annual total cost per patient varying from 170,000 to 600,000 baht, with medication costs constituting the largest portion[4]. In addition, hepatitis is a stigmatized disease while HCC is associated with debilitating symptoms that significantly impact patients' quality of life (QoL).

While NASH and NAFLD are an emerging concern globally and may contribute to HCC development, viral hepatitis, particularly HBV and HCV, remains the primary cause of HCC in APAC, contributing to a significant proportion of liver cancer cases in the region[5].

Given the high prevalence and strong association between viral hepatitis and HCC, it becomes crucial to prioritize interventions, such as surveillance programs, that specifically target this population so that efforts can be concentrated on early detection, timely interventions, and appropriate management strategies to reduce the burden of HCC and improve patient outcomes in the region. This focused approach allows us to delve deeper into these specific topics, providing in-depth analysis and insights that can be directly applied to enhance interventions.

For these reasons, this white paper aims to provide evidence-based recommendations to reduce the clinical, economic, societal, and humanistic burden of hepatitis and HCC and improve patient outcomes in the APAC region.

3.2 HEPATITIS IS ASSOCIATED WITH HIGH MORTALITY, MORBIDITY AND ECONOMIC LOSS

Hepatitis deaths in APAC have reached 1 million per year, a death rate three times higher than deaths from HIV/AIDS, and accounting for 63% of the global death toll from the disease. China and India alone have a combined estimate of 182 million people chronically infected with HBV or HCV[6].

The persistently low levels of awareness of screening, at-risk populations, and treatment options for HBV and HCV has led to the continued transmission of viral hepatitis, with a staggering 90% of those infected remaining undiagnosed[7,8].

Social stigma associated with hepatitis, coupled with depression and anxiety, are key causes for under-diagnosis, and further exacerbate the problem by creating barriers for patients to seek treatment[7,9]. For example, job or school applicants may be denied employment or placement in Philippines and China if they test positive for hepatitis B[10]. This is particularly true for marginalized communities, including people who inject drugs (PWID), men who have sex with men (MSM), incarcerated individuals, commercial sex workers (CSW), people with sexually-transmitted infections (STI) and people living with HIV (PLHIV), all of whom are at an increased risk of viral hepatitis[10].

Given the heavy burden of disease in the region, there is an urgent need to stem the spread of hepatitis. Prevention is vital to protect society as a whole and avert the emergence of severe complications, such as HCC[11]. In addition, the barriers to treatment mean that concerted efforts must be made to enhance public awareness and improve access and availability of screening, diagnostic testing and treatment, with the ultimate aim of eliminating this disease from our communities.

THE SIGNIFICANT ECONOMIC BURDEN IMPOSED BY HEPATITIS

Vietnam

Studies have highlighted the significant economic burden imposed by hepatitis and hepatocellular carcinoma (HCC), particularly in Vietnam. A standard twelve-week course of sofosbuvir and daclatasvir for Hepatitis C (HCV) can cost up to US$2,472 in Ho Chi Minh City in 2019[12] and out-of-pocket expenditure can range from 47% to 100% of total treatment costs[13]. This expenditure is comparable to 3 to 6 months of the average monthly personal income in Vietnam[13]. HCC treatment with Transarterial Chemoembolization using Lipiodol (cTACE) and drug-eluting bead (DEB-TACE) in Vietnam had an out-of-pocket cost of US$237 to US$294 per bottle of Lipiodol and bead respectively in 2018[14,15]. These findings underscore the substantial financial strain associated with managing this disease in a developing country with a gross domestic product of approximately US$4,110[16] per-capita.

Australia

Research conducted in Australia has revealed that if significant treatment scale-up is not implemented, the economic burden of Hepatitis C (HCV) could be severe[17]. The estimated cost of direct health expenses related to testing, treatment, and disease management is AUD 3.0 billion between 2016-2030[17]. Moreover, the impact of hepatitis C on the economy is significant, with an estimated AUD 26 billion in lost productivity due to HCV-related absenteeism, presenteeism, and premature deaths[17]. These findings underscore the critical importance of prioritizing measures to prevent and manage HCV to mitigate its significant burden on the healthcare system and the wider economy.

3.3 EFFORTS TOWARDS ELIMINATING HEPATITIS NEED TO BE INTENSIFIED

In 2016, the World Health Organization (WHO) Global Health Sector Strategy (GHSS) on viral hepatitis set out an ambitious target to eliminate viral hepatitis as a public health problem by 2030, through a 90% reduction in incidence and a 65% reduction in mortality, compared with a 2015 baseline[18]. The Sustainable Development Goals (SDG) in the UN's 2030 Agenda for Sustainable Development mirror these targets, underlining the urgency and importance of eliminating HBV and HCV as a public health problem[1].

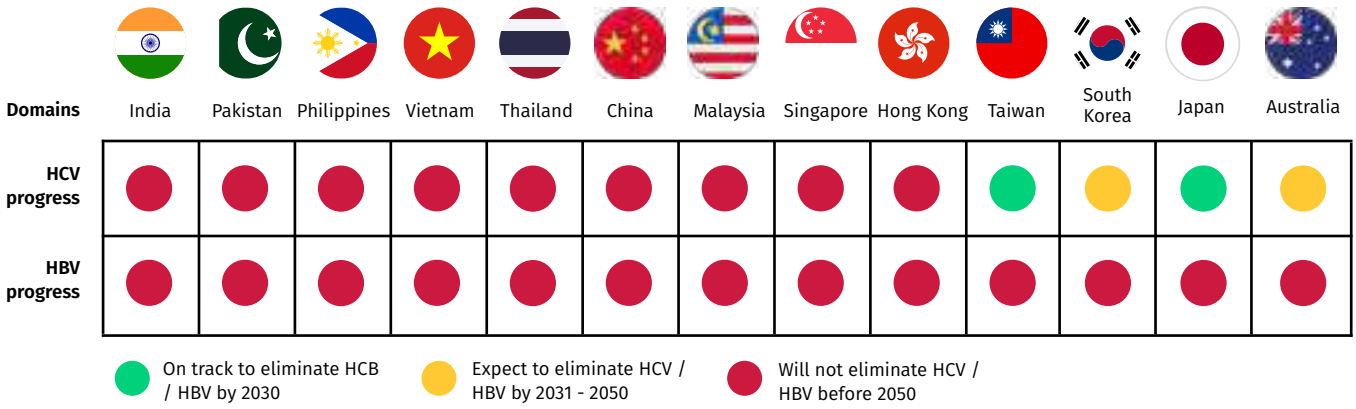
In 2021, the WHO followed up with their Guidance for country validation of viral hepatitis elimination, providing a framework for territories to measure their efforts in reducing both new infections of HBV and HCV and deaths from liver cirrhosis and cancer, along with reaching high coverage (>90%) of program interventions, to confirm attainment of elimination[18].

Eliminating hepatitis in 67 low- and middle-income territories, which accounts for 75% of the word's population, would prevent the deaths of 4.5 million people by 2030[19]. There is also compelling evidence demonstrating the cost savings:

Every dollar spent on HBV elimination activities yields a two to four times return on investment[20]. HCV elimination would also avert 2.1 million deaths globally, generating USD 46.1 billion in cumulative productivity gains and become cost-saving in 4 years, with a net economic benefit of USD 22.7 billion by 2030[21].

Despite this guidance and evidence, most APAC territories studied are not on track to eliminate hepatitis by 2030 (see ***Figure 1*** – the rationale for focusing on these 13 territories is detailed in ***Section 4: Methodology***.) Only a minority of territories, such as Taiwan, have made notable progress towards eliminating HBV and HCV by 2030 and serve as sources of best practices for other territories in the region[22].

Figure 1: *Progress of various APAC territories towards WHO hepatitis elimination goal based on the modelling by the CDA Foundation which forecasts the year in which each territory will achieve WHO 2030 elimination targets[22]*



The lack of progress towards eliminating hepatitis by 2030 points to the need for APAC territories to increase their efforts to scale up hepatitis testing and treatment to meet the WHO targets. HBV elimination progress is also lagging behind HCV and this can be attributed to the lack of a cure for HBV. In turn, this has led to lower awareness and civil society movements to drive advocacy for HBV[23]. HBV monitoring is also more complex (involving many steps) and hence more challenging than HCV[23]. The absence of an HCV vaccine further hinders efforts to eradicate hepatitis, adding to the existing challenges.

That said, the elimination of hepatitis is a challenging but achievable goal. This white paper will explore the challenges and opportunities that exist in the region and will examine the best practices and case studies of territories that have made progress in eliminating hepatitis and tackling HCC. By sharing knowledge and experience, we hope to promote greater understanding and collaboration between stakeholders in the fight against hepatitis and HCC in the APAC region.

3.4 HCC IS CAUSED BY HBV AND HCV, BUT CONTINUES TO BE DIAGNOSED LATE AND IS THE SECOND DEADLIEST CANCER IN APAC

HCC presents a severe and potentially life-threatening condition that poses a significant public health challenge in the APAC region. Liver cancer (predominantly HCC) is the fifth most prevalent cancer and the second deadliest one in APAC[24]. HBV and HCV are the leading causes of HCC in the region[25].

More concerning still, the trend is worsening; the year 2020 alone saw about 609,500 new cases of HCC in Asia, accounting for a staggering 73% of the total incidence of HCC worldwide[24]. In addition, HCC-related deaths in Asia were estimated to account for 72% of the total HCC deaths worldwide, with a harrowing number of 566,000 reported cases[24]. These figures highlight the alarming and growing impact of this disease on the APAC region.

More than 80% of HCC cases in APAC are diagnosed at a late stage when the disease has already advanced, making it challenging to achieve curative outcomes, despite the availability of effective treatment options[26].

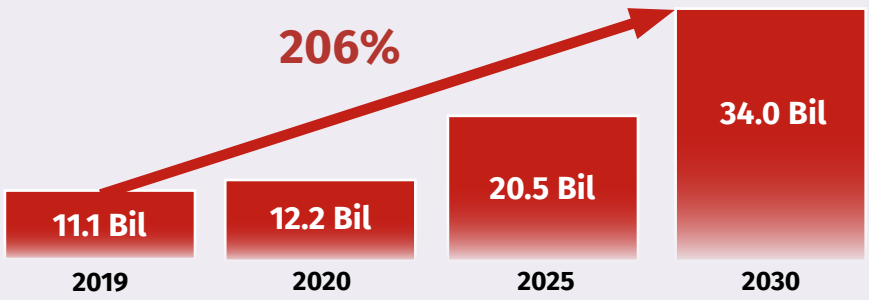
This contributes to HCC's position as the second most common cause of premature mortality from cancer[27]. In addition to the physical suffering experienced by HCC patients, including symptoms such as abdominal pain, weakness, fatigue, and loss of appetite, there is also a significant economic burden associated with this disease[28].

Several studies have highlighted this economic burden associated with HCC in the APAC region.

ECONOMIC BURDEN ASSOCIATED WITH HCC IN ASIA PACIFIC

In China, the overall economic burden of liver cancer was estimated at US$11.1 billion in 2019, equivalent to 0.047% of the local GDP[29]. This economic burden includes both direct and indirect costs, with direct expenditure estimated at US$3.1 billion, comprising US$2.9 billion in medical expenditure and US$0.3 billion in non-medical expenses[29]. The indirect cost was estimated at US$8.0 billion, including US$0.4 billion due to disability and US$7.5 billion due to premature death[29].

The total economic burden of liver cancer in China is projected to increase to US$12.2 billion, US$20.5 billion, and US$34.0 billion in 2020, 2025, and 2030, respectively, accounting for 0.102%, 0.138%, and 0.192% of China's GDP[29]. These findings illustrate the substantial financial burden of HCC in the APAC region and the need for targeted efforts to reduce its economic impact.



Given the substantial economic burden and high mortality rates associated with HCC in the APAC region, it is essential to prioritize the disease from end to end of the patient journey; from prevention and early detection to effective treatment strategies. This will require concerted efforts by stakeholders across multiple sectors, including public health agencies, healthcare providers, policymakers, patients and industry, to raise awareness and promote access to timely and appropriate care.

Addressing the underlying risk factors for viral hepatitis, including promoting vaccination against HBV, reducing the incidence of HCV through targeted prevention strategies such as systematic and targeted screening, comprehensive harm reduction services and increasing access to affordable and effective treatments, through integrated, person-centered delivery models (which engage individuals in healthcare provision and account for individuals' needs, values and disease experience), are essential steps in reducing the prevalence and impact of HCC in the APAC region[24]. This points to the importance of viral hepatitis management as the first prevention for HCC, but once the disease has progressed to HCC, having an effective national surveillance program also plays a crucial role. This facilitates early detection, allowing for timely interventions and potentially improving patient outcomes, as well as monitoring of high-risk populations.

3.5 A COMPREHENSIVE POLICY SHOULD COMBINE HEPATITIS ELIMINATION AND HCC CONTROL WITHIN THE UHC FRAMEWORK

Despite the high prevalence of these liver diseases, they often do not receive the necessary attention as they are overshadowed by other infectious and chronic diseases, such as HIV[30].

Presently, most global, regional and national organizations and initiatives focus on only one of hepatitis or HCC (see ***Figure 2***)[31]. This siloed approach results in inadequate and poorly funded policy response of most governments to hepatitis and HCC[31,32]. It also fails to address or leverage the high mortality, morbidity and economic loss associated with these diseases[31,32].

Figure 2: *Examples of global, regional and national organizations for liver diseases*

Global Organizations

- Assist in **planning, implementation** & **evaluation of national** & subnational programmes
- Tend to focus on **specific diseases** within the liver disease continuum

Regional Organizations

- Multidisciplinary body **advocating** public policy reforms and involved in **promoting** prevention, implementation & community mobilization programmes

National Organizations

- Several local & national **alliances**, associations and patient groups targeting different liver conditions
- Highly fragmented with **significant** inter- and intra-country variations

A policy response that combines hepatitis elimination and HCC control efforts can help to synergize efforts and reduce the economic and health burdens associated with both diseases[31,32]. Viral hepatitis elimination also meets all the criteria for inclusion in the UHC framework[33]. This means that while catalytic funding will be crucial to set up and implement national action plans in less developed territories, viral hepatitis and HCC response should be incorporated into broader UHC programs funded by national funders and international donors such as The Global Fund[33].

As the first platform to address a wide range of liver diseases, including hepatocellular carcinoma and viral hepatitis in the APAC region, the APAC Liver Disease Alliance is well placed to build on the work of organizations such as APASL and CEVHAP which have a long history in APAC.

Early detection and treatment can also play a critical role in reducing mortality and economic loss associated with hepatitis and HCC. Moreover, there are tools available to eliminate hepatitis, which is a primary cause of HCC, and to implement best practices for managing HCC, based on Japan's experience and the Japan Society of Hepatology Clinical Practice Guidelines[34–37]. Japan is widely acknowledged as a global leader in the management of HCC[36]. The outcomes of their HCC practice provide evidence that HCC interventions can result in significant economic savings and improved health outcomes for both HCC and hepatitis patients[34–37].

In the following sections of this paper, we will elaborate on the current landscape, best practices, and the case for investment.

04 Methodology

This White Paper does not aim to provide an exhaustive review of all territories; rather, its focus is to shed light on the current landscape and best practices from selected territories for the benefit of all stakeholders. To achieve this, the paper draws on a wide range of sources, including literature reviews, workshops, and roundtable discussions with experts in the field of hepatitis and HCC.

Given the diversity and number of territories across the APAC region, it is simply not feasible to include every territory in one paper. We have thus focused on 13 territories (see ***Figure 3***) when assessing the HBV, HCV and HCC landscape to reflect the full spectrum of healthcare system maturities, funding approaches, and HCC and hepatitis management differences in APAC. However, we have also assessed best practices from other territories within and beyond APAC (e.g. Cambodia and Egypt) when formulating the key policy recommendations as their experiences contain valuable learning points for territories across APAC.

We focus on 13 territories to reflect the full spectrum of healthcare system maturities, funding approaches, and management differences in APAC.

Figure 3: *The 13 APAC territories analyzed in this white paper*

To gather relevant information in all territories, we conducted a targeted literature review of international and national sources in journal publications and symposiums such as the Hepatitis C Virus Elimination Symposium and Solidarity for Hepatitis Elimination. The information we gathered was then organized into three themes: (1) the need to address hepatitis and HCC together; (2) progress made and gaps in international and national efforts to tackle hepatitis and HCC; and (3) best practices from successful case studies.

The challenges and recommendations outlined in this White Paper were developed and refined through the collaborative efforts of leading hepatitis and HCC experts.

This process included a Liver Alliance Charter workshop, as well as a roundtable discussion focused specifically on identifying and addressing the key challenges and opportunities in the field. The insights gathered from these discussions were then used to inform our landscape assessment and policy recommendations, ensuring that our findings are grounded in the latest research and expert perspectives.

To evaluate the landscape of hepatitis and HCC, we created a scorecard that employs indicators to measure policy and implementation factors linked to better outcomes, as cited in research publications or authoritative sources such as the Coalition for Global Hepatitis Elimination country dashboard, national hepatitis action plans for hepatitis, or clinical practice guidelines on the management of HCC.

Leading hepatitis and HCC experts reviewed and advised on the development of the scorecard through the roundtable discussion mentioned above, one-on-one discussions and email correspondence. Through this process, we identified a set of 6 HCC indicators and 7 hepatitis indicators to evaluate each territory across the 4 domains. Full explanations of the scorecard methodology are available in the appendix.

Hepatitis	
Domain	**How each domain was assessed**
Comprehensive national action plan	▸ Presence of a National Action Plan for HBV ▸ Clear goals and targets aligned with WHO elimination indicators to reduce the burden of HBV and HCV
Sustainable and strong funding and access	▸ Clear budget allocation or financial plan within the National Action Plan ▸ Extent of national or state/provincial government funding/reimbursement for prevention, screening, diagnosis and treatment of HBV and HCV
Strong political Commitment	▸ Progress towards eliminating HBV and HCV by 2030 ▸ Strong institutional commitment towards eliminating HBV and HCV in the form of a government agency that coordinates the national multisectoral hepatitis elimination effort ▸ Government support in the form of national policies, partnerships or initiatives to eliminate hepatitis in the past 2 years
Good implementation of the national plan or hepatitis elimination efforts	▸ High nationwide uptake of the HBV birth dose vaccination ▸ Hepatitis elimination initiatives tailored to different populations (e.g. vulnerable high risk groups like pregnant mothers and marginalized high risk groups like PLHIV, MSM etc) rolled out nationwide ▸ High diagnosis rate and treatment uptake

HCC	
Domain	**How each domain was assessed**
Comprehensive national action plan	▸ Presence of a national population-based HCC surveillance program ▸ Inclusion of liver cancer in the national cancer control plan
Sustainable and strong funding and access	▸ Extent of national or state/provincial government funding/reimbursement for screening and treatment of HCC
Strong political Commitment	▸ Strong institutional commitment in the form of a national organization (backed by the government) that coordinates or supports HCC control efforts nationwide ▸ Government support in the form of national policies, partnerships with industry or NGOs or clinical research bodies etc to control HCC in the past 2 years
Good implementation of HCC control efforts at a national level	▸ Presence of comprehensive guidelines for HCC diagnosis/screening, monitoring, surveillance and treatment ▸ Clearly defined high risk groups (cirrhotic patients and patients with chronic HBV or HCV) who should be recommended HCC surveillance ▸ HCC surveillance and diagnosis with ultrasound and 3 biomarkers (AFP, PIVKA- II, AFP L3) every 3-4 months for extremely high-risk patients or every 6 months for high risk patients as per the Japan Society of Hepatology Clinical Practice Guidelines for Hepatocellular Carcinoma

05 HBV, HCV and HCC landscape assessment of select APAC territories

5.1 KEY CHALLENGES IN THE HEPATITIS AND HCC PATIENT JOURNEYS

1. HCV & HBV screening and diagnosis:

- Lack of national hepatitis screening program (currently limited to opportunistic screening in all except TW and JPN)
- Patients' unwillingness to accept testing ('head in the sand' mentality)
- HBV screening is not included in antenatal care programs
- Low disease awareness
- Poor access to testing
- Stigma associated with hepatitis

2. HCV & HBV treatment:

- Poor linkage to care
- Poor treatment access
- Lack of curative HBV treatment

3. HCV & HBV monitoring:

- Poor patient compliance to chronic HBV treatment and monitoring

4. HCC surveillance:

- Lack of sufficient awareness regarding the significance of HCC surveillance
- Disparity in surveillance practices between urban and rural areas
- Poor patient compliance
- Poor access
- Suboptimal performance of current surveillance tools

5. HCC prognosis:

- Majority diagnosed at late stage
- Lack of curative treatment at late stage
- Poor access to diagnostic imaging modalities

6. HCC treatment:

- Lack of efficacy and poor QoL
- Poor access to targeted or immunotherapies

5.2 GAPS IN HBV AND HCV POLICY, FUNDING, SCREENING AND LINKAGE TO CARE

5.2.1 WHAT IS NEEDED FOR SUCCESS?

Before we look at the individual gaps in selected territories, it is helpful to frame what a successful, or "gold standard" strategy and implementation for hepatitis elimination looks like. Based on our research and discussions with experts, we believe the following four factors are the key to hepatitis elimination:

The presence of a national plan for HBV and HCV

This provides the frame for all stakeholders by setting clear and common time-limited quantitative targets and details the programs and funding required to achieve these targets. Research has shown that meeting these targets will improve clinical and social outcomes (as detailed later in this section) and lead to economic benefit (as detailed in ***section 6***)

Sufficient political will and coordination

Crucial to secure buy-in of all relevant stakeholders for effective implementation (including government funding) of programs within the framework of national plans.

Adequate funding

Sustainable government funding is essential to kick-start and maintain hepatitis programs within the framework of national plans and/or broader UHC programs; in less developed territories, catalytic funding from international donors can help to kick-start programs and generate momentum to secure government funding.

Well-established health services, especially screening programs, integrated within existing health systems and tailored to the needs of affected populations in different settings

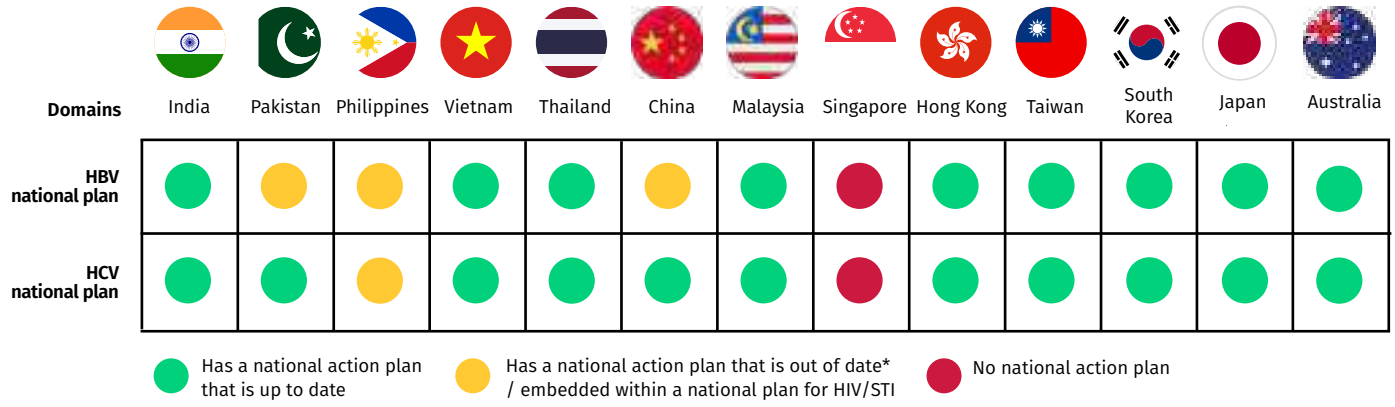
Essential to identify reservoirs of infection and break the chain of infection by ensuring that infected individuals are detected early and referred for confirmatory diagnosis and treatment, especially in marginalized and stigmatized populations (such as PWID) with lower screening and higher drop-out rates; HBV screening and treatment remain essential even if HBV birth-dose vaccination is available due to variable vaccination coverage across APAC.

In the next sections, we will look at different territory examples that highlight the successes and shortcomings in each of these four factors, and where gaps remain across the APAC region.

5.2.2 THE PRESENCE OF A NATIONAL PLAN FOR HBV AND HCV

Broadly, territories can be categorized into those that do not have plans, those that have an outdated plan (e.g. the National Hepatitis Elimination Country Profile by the Coalition for Global Hepatitis Elimination noted that National Hepatitis Plan for Pakistan has not been updated since 2021), and those with up-to-date plans (defined active as of 2022 inclusive) (see ***Figure 4*** below). All territories with an up-to-date national hepatitis action plan also cite the WHO hepatitis elimination targets in their plans[38]. While the presence or absence of a national plan does not correlate to the income status of the territory, it does correlate to political priority.

Figure 4: *Status of national plan for HBV and HCV*[1,38–41]



*As defined by the National Hepatitis Elimination Country Profile by the Coalition for Global Hepatitis Elimination

For example, affluent Singapore does not currently have a hepatitis national plan as HCV and HBV are considered lower health priorities based on the low prevalence of HCV in the general population (see ***Table 1***) and high HBV birth vaccination dose coverage of 91%[39]. At the other end of the wealth spectrum, India does have a current plan, with viral hepatitis as one of its top health priorities, despite much lower funding for healthcare per capita.

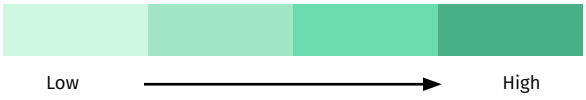
Table 1: *Incidence and prevalence of HBV and HCV by territory*

Territories	Hepatitis B		Hepatitis C	
	Incidence*	Prevalence	Incidence*	Prevalence
Singapore	0.90[42]	3.60%[43]	0.20[42]	0.10%[43]
China	69.25[44]	5.02%[45]	15.09[46]	0.91%[47]
India	N/A**	3.00%[48]	N/A**	0.50%[49]
Thailand	N/A**	5.10%[50]	N/A**	1.00%[51]
Vietnam	N/A**	9.40%	N/A**	1.80%
Japan	N/A**	0.90%[52]	0.40[53]	0.13%[53]
Republic of Korea	0.71[54]	2.90%[55]	11.9[54]	0.90%[55]
Philippines	N/A**	10.00%[56]	N/A**	0.60%[56]
Malaysia	N/A**	1.70%[57]	N/A**	0.40%[57]
Taiwan	0.61[58]	N/A**	2.39[58]	3.28%[59]
Australia	23.2[60]	0.90%[60]	36.6[60]	0.05%[60]
Pakistan	N/A**	1.10%[61]	N/A**	4.30%[61]
Hong Kong	N/A**	7.20%[62]	N/A**	0.30%[62]

**Per 100,000 population in all territories except Japan, where data was captured per 100,000 people years*

***No publicly available data on Hepatitis B and C incidence in this territory at the time of publication*

Colour legend



Territories without national hepatitis plans or up-to-date national plans (such as Singapore and Pakistan) are more likely to lack coordinated and well-resourced hepatitis elimination programs. Hepatitis programs in these territories are thus limited to HBV newborn vaccination programs and/or initiatives led by NGOs or provincial/state governments[63]. For instance, in the case of Pakistan, Aga Khan University (AKU), a renowned private international university, has led pilot HCV micro-elimination efforts in three Union Councils (UC) of Malir District, Karachi in 2022[64]. Similarly, in Singapore, its first HCV elimination initiative has been introduced through a public-private partnership model to provide HCV testing and linkage to care services for high-risk populations[65]. Although these targeted initiatives are commendable and can provide a starting point, it is crucial to prioritize the scaling up of these efforts.

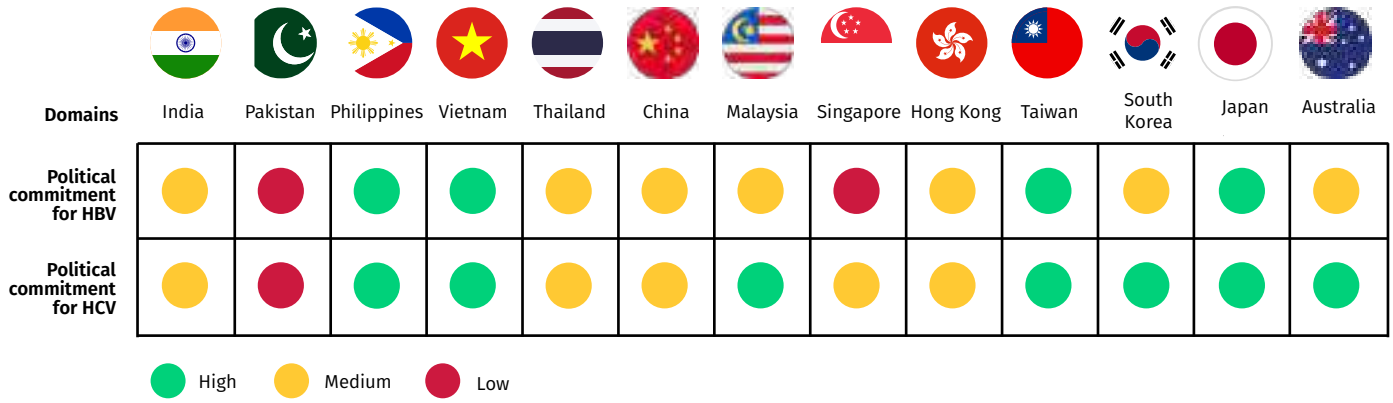
A national hepatitis plan is recognized by experts as a pre-requisite to eliminate hepatitis, but it is not a guarantee[23].

A national hepatitis plan is crucial for the successful elimination of hepatitis as it serves as a foundational framework, providing clear goals, targets, and actionable steps towards achieving this goal. However, it is also not a guarantee that a plan will translate to results all the time. While Taiwan and Japan – the only territories on track to eliminate HCV by 2030 – have national hepatitis plans, so do territories like Australia, South Korea, Malaysia, Thailand and Vietnam – all of which are not on track to eliminate by 2030[1,38–41]. It is also worth recognizing that most countries are not on track for HBV elimination within the same timeframe. In assessing whether a territory is on track to hepatitis elimination, we used data from The Polaris Observatory. CDA Bright (HCV) and PRoGReSs (HBV) models were utilized to predict the attainment year of WHO's 2030 elimination targets for each territory, including diagnosed cases, treatment coverage, mortality reduction, and incidence reduction, which is then compared against the WHO's 2030 goal. Taiwan and Japan's national hepatitis plans stand out for being comprehensive and are characterized by strong political will and coordination, sustainable domestic funding, universal screening and strong linkage to accessible, high-quality care. This points to the need for territories to be proactive and take the next step to ensure that national action plans are adequately funded and implemented. We will examine these and the critical success factors leading to Taiwan's and Japan's success below and in the key policy recommendations later in this paper.

5.2.3 SUFFICIENT POLITICAL WILL AND COORDINATION

Political will and commitment (see ***Figure 5***) are assessed by the progress that each territory has made towards eliminating hepatitis by 2030, the presence (or absence) of a dedicated national hepatitis taskforce, ministry, or agency indicating institutional commitment and government support for policies, partnerships or initatives to eliminate hepatitis in the past 2 years.

Figure 5: *Level of political commitment to eliminate hepatitis across 13 APAC territories*



Political will and coordination are crucial determinants of successful policy development and implementation. Pakistan's experience demonstrates this. Firstly, the HBV newborn vaccination mandated by the national government in Pakistan is still not available in all provinces[61], underscoring the lack of coordination across national, provincial and local governments. Secondly, an ambitious screening and treatment program for hepatitis in 2019 was announced by the former Pakistan Prime Minister, Imran Khan[61]; however, it remains unclear when the above-mentioned program will be launched due to a resource re-allocation following the COVID outbreak in 2020-2022[66], followed by a change in Prime Minister in 2022.

The political sensitivity and stigma associated with populations at increased risk of hepatitis such as PWID have also dampened politicians' willingness to support hepatitis screening and treatment programs for these marginalized groups in Singapore and Philippines[67–69]. Encouragingly however, the Singapore government has recently relaxed its stance by publicly endorsing an NGO-led pilot program to screen and treat previously incarcerated persons for HCV[70].

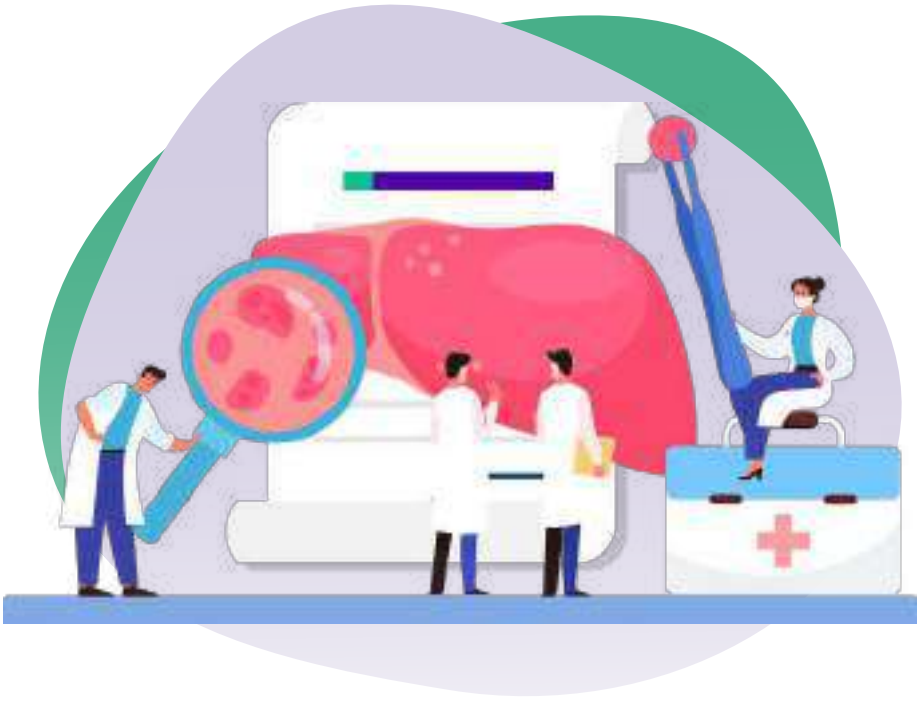
However, political will and coordination alone are not enough to allow a territory to eliminate hepatitis by 2030. Among the territories with higher political will, only Taiwan and Japan are on track to eliminate HCV by 2030[1,38–41]. This suggests that other factors such as adequate funding must also be fulfilled for successful policy implementation and hepatitis elimination by 2030. For resource-limited territories like India, Pakistan, Vietnam and Philippines, demonstration of political will in the form of initial action being taken towards implementing a national plan is also the first step towards securing catalytic funding from global donors such as The Hepatitis Fund[21,75].

BOX 1: TAIWAN CASE STUDY
Strong political commitment drove prompt and swift response plans for HCV[72,74]

Upon the launch of WHO's goal in 2016, a series of expert meetings has been held, establishing policy guidelines, thus reflecting strong government support right from the start. With this, the National Hepatitis C Program (NHCP) office was set up in Dec 2016 under the guidance of MOHW.

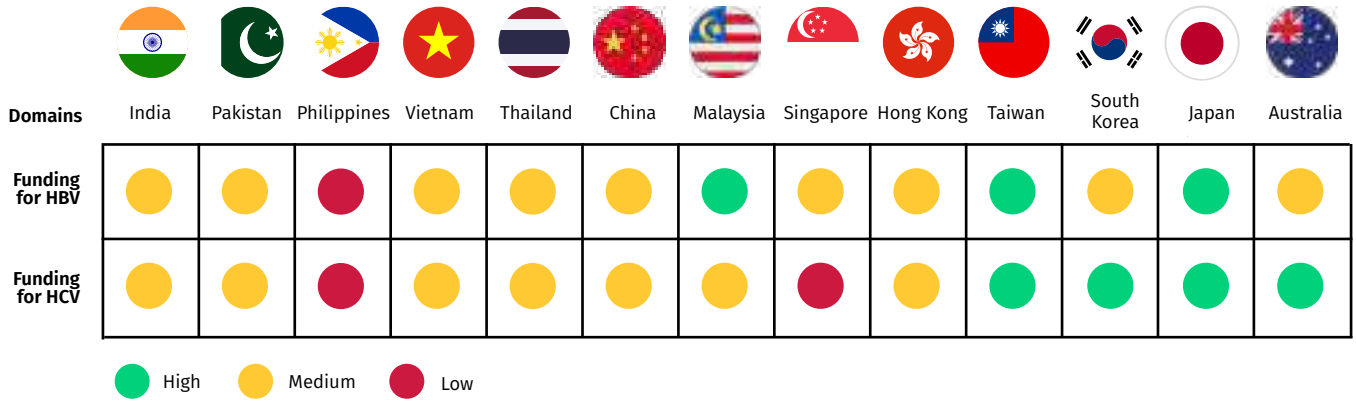
After 2 years, efforts from various stakeholders including experts, public health officers, legislators and government leaders have culminated in Taiwan's Hepatitis C Policy Guideline 2018-2025 which demonstrates political commitment by MOHW to eliminate HCV by 2030 through active screening and relaxation of treatment reimbursement criteria whilst ensuring sustainable financing.

However, political will and coordination alone are not enough to allow a territory to eliminate hepatitis by 2030. Among the territories with higher political will, only Taiwan and Japan are on track to eliminate HCV by 2030[1,38–41]. This suggests that other factors such as adequate funding must also be fulfilled for successful policy implementation and hepatitis elimination by 2030. For resource-limited territories like India, Pakistan, Vietnam and Philippines, demonstration of political will in the form of initial action being taken towards implementing a national plan is also the first step towards securing catalytic funding from global donors such as The Hepatitis Fund[21,75].



5.2.4 ADEQUATE FUNDING

Figure 6: *Funding for hepatitis elimination across 13 APAC territories*



Despite the formulation of national plans to achieve the World Health Organization (WHO) goals of eliminating viral hepatitis in approximately 70% of territories/regions worldwide by 2017, fewer than 50% of territories have allocated adequate funding for implementation[76]. For instance in India (see ***Figure 6*** above), HCV lacks the necessary domestic and international interest and hence, resources to finance commodities and programming for elimination at a national level[77]. WHO has also highlighted the need for increased investment in hepatitis elimination in Vietnam[78].

Adequate funding to eliminate hepatitis needs to cover screening and treatment for effective service delivery.

The recent identification of novel HBV biomarkers such as quantitative HBV surface antigen (qHBsAg), hepatitis B RNA (HBV RNA) and core-related antigen (HBcrAg), have demonstrated potential in a range of clinical settings. They hold the promise of improving early detection, stratifying the risk of future complications and therapeutic monitoring of HBV-infected individuals[79]. These advancements serve as a reminder that the field of hepatitis is continually evolving, with exciting improvements on the horizon. Therefore, it is important to acknowledge that the implementation of these advancements will require dedicated funding efforts to ensure patient access.

Australia, Japan, Taiwan and to a lesser extent Hong Kong and South Korea have all set aside funding to ensure successful implementation of their respective national hepatitis plans. Free HCV screening is available nationwide in Japan[71], Taiwan[72] and Australia[80]. There is also unrestricted access to DAA (Direct-acting antivirals) in territories like Australia and Taiwan[81]. The Hong Kong government has also set aside a USD120m recurrent budget to cover the cost of DAA for 1,700 HCV patients annually[82] while DAA is reimbursed in South Korea, albeit with a hefty out-of-pocket co-pay cost of up to USD3,000[83].

However, funding often falls short of covering the entire hepatitis national plan in less affluent territories and this was exacerbated by the COVID-19 pandemic that emerged in 2020[76]. The pandemic diverted the attention of governments and intensified competition for previously allocated resources and funding, delaying progress in hepatitis elimination efforts[76].

A case in point would be the experience of Pakistan where an ambitious screening and treatment program for hepatitis announced in 2019 is still awaiting funding to start[61]. Likewise in Philippines, the COVID-19 pandemic has slowed efforts for expanding a service delivery model for HBV in the public sector[84]. As a result, most of the screening, diagnosis, and treatment activities for HBV remains largely concentrated in the private sector in Philippines[84].

Furthermore, viral hepatitis lags other infectious diseases in terms of funding, with no equivalent to initiatives like the President's Emergency Plan for AIDS Relief (PEPFAR) for hepatitis and limited support from The Global Fund in the fight against viral hepatitis[76].

The chronic lack of funding for hepatitis programs globally is largely driven by a lack of public awareness regarding the significant disease burden of viral hepatitis, which hampers efforts to secure funding from key stakeholders[76]. There is thus a pressing need to raise awareness about the severity of viral hepatitis as a disease and its impact.

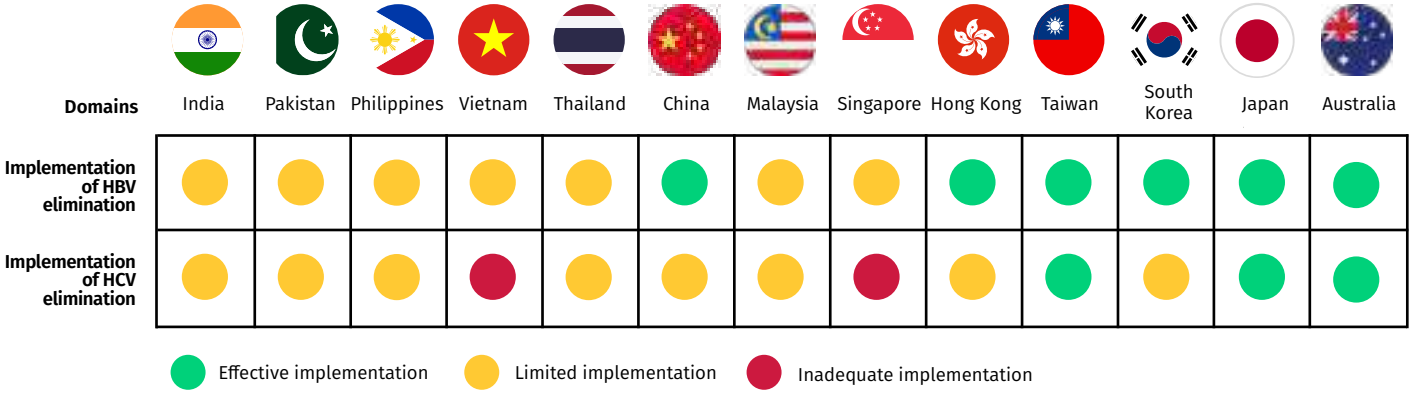
Although funding from organizations like The Global Fund and Unitaid has provided some support for addressing HIV and key populations (such as those living with HIV, people who inject drugs, and pregnant women), the funding allocated for addressing the burden of hepatitis has been limited and insufficient[75], especially in APAC which accounts for the bulk of the global hepatitis death toll. Inadequate domestic healthcare funding has also been widely acknowledged as a key barrier to implementing national hepatitis elimination plans[75]. However, even small incremental investments – as little as USD250,000 – from global funders can have a significant impact[85]. During the COVID-19 pandemic, the Hepatitis Fund issued first-round grants to organizations to scale up hepatitis programs in Pakistan and Vietnam[85]. These investments have created demonstrable change in lower out-of-pockets costs, increased human resources capacity, and helped governments to unlock domestic resources for hepatitis elimination[85]. These have since led to reimbursed HCV confirmatory testing outside of hospitalization in Vietnam and 461 primary care centers offering HCV screening in Pakistan[85].

There is also an opportunity to incorporate viral hepatitis response into broader UHC programs funded by national funders and international donors such as The Global Fund as viral hepatitis elimination meets all the criteria for inclusion in the UHC framework[33]. This includes integrating viral hepatitis programs with existing testing and treatment services including HIV and tuberculosis[86].

Lower-middle income territories such as Vietnam (HCV) and Philippines (HBV) have begun to explore the integration of viral hepatitis response within programs that are already funded by The Global Fund and other funding agencies (e.g. HIV programs)[76]. Vietnam has successfully leveraged this, demonstrated by the successful acquisition of US$1.2 million under the 2018-2020 GFATM HIV grant., enabling the provision of 16,000 DAA treatment courses for PLHIV co-infected with HCV[87]. Furthermore, catalytic investments can jumpstart the planning and management of hepatitis response programs. Encouragingly, Thailand[88], Vietnam[89] and India[77] have all implemented pilot programs within the framework of national hepatitis programs (with the support of international partners like PATH, DNDi, CHAI, The Global Fund and The Hepatitis Fund) to generate cost effectiveness data and secure future government funding to expand these programs nationwide.

5.2.5 WELL-ESTABLISHED HEALTH SERVICES, ESPECIALLY SCREENING PROGRAMS, INTEGRATED WITHIN EXISTING HEALTH SYSTEMS AND TAILORED TO THE NEEDS OF AFFECTED POPULATIONS IN DIFFERENT SETTINGS

Figure 7: *Implementation of hepatitis elimination initiatives across 13 APAC territories*



Only Taiwan and Japan have national general population HBV/HCV screening programs (see ***Figure 7*** above). Most of the other territories only have HBV/HCV micro-elimination screening programs for PLHIV, PWID or pregnant women.

Insufficient integration of hepatitis services such as screening into universal health coverage initiatives and the lack of HBV screening as part of antenatal care programs and political sensitivity associated with supporting marginalized populations at risk of HCV.

However, hepatitis patients in almost all territories do not receive equitable care throughout their journey due to persisting barriers to access care[92]. This is hampered further by insufficient integration of hepatitis services such as screening into universal health coverage initiatives and the lack of HBV screening as part of antenatal care programs (thus missing the opportunity to break the mother-to-child transmission chain of hepatitis alongside HIV and syphilis[86,92]), and political sensitivity associated with supporting marginalized populations at risk of HCV.

Despite ongoing efforts to eliminate hepatitis, there are still "missing millions" who remain undiagnosed, untreated, and left to live with the disease without proper assistance[10,93]. These individuals may be found in the general population and marginalized communities with suboptimal access to care (e.g. PWID, men who have sex with men (MSM), people who live with HIV). The latter group tends to experience worse health, social and economic outcomes due to loss of education, marriage, employment opportunities[10]. Crucially, these marginalized communities may also represent hidden reservoirs of infection and targeted interventions for these groups can serve to interrupt and prevent onward transmission.

Addressing issues within marginalized communities is challenging due to political sensitivity which leads to a deprioritization of viral hepatitis elimination[94]. Despite being at an increased risk of viral hepatitis, marginalized populations often face disproportionate barriers to accessing effective hepatitis treatment solutions due to double stigma – both as part of a risk group and as individuals with hepatitis[10,93]. They experience suboptimal preventive measures, treatment deliveries, and disease management, and lack outreach programs for on-site HCV and HBV testing to link them to care[95].

The importance of screening and linkage to care for marginalized populations at risk of hepatitis is underscored by Australia's experience where DAA have mostly been prescribed to older patients who have been diagnosed with hepatitis for some time while diagnosis and treatment uptake among younger people with newly acquired infections (typically PWID) remains low[96]. This has occurred despite the availability of reimbursed DAA without restrictions, and leaves Australia at risk of missing its goal of eliminating hepatitis by 2030. Stepping up targeted screening for younger patients and strengthening linkage to care to ensure those diagnosed with hepatitis are treated with DAA will be crucial to reaching its targets[96].

Hong Kong[82], Malaysia[95], Taiwan[74], Australia[97] and Singapore[70] have implemented or are considering implementing hepatitis screening and linkage to care services (direct referrals to hospitals) for PWID or people previously in closed settings; however, screening and linkage to care for marginalized populations remain key challenges in hepatitis elimination efforts in most territories.

5.3 GAPS IN HCC SURVEILLANCE AND FUNDING

5.3.1 WHAT IS NEEDED FOR SUCCESS?

Japan is internationally perceived as an exemplar in HCC surveillance and management[36,37]. Based on our analysis of Japan's HCC surveillance model and discussions with key opinion leaders in HCC, we have identified the following critical success factors for effective HCC surveillance and management[36,37]:

Presence of a National HCC surveillance program

Ensures that surveillance of HCC is implemented nation-wide to detect HCC early and track program outcomes such as cancer stage at diagnosis and 5-year survival rate.

Sufficient political will and coordination

Crucial to secure buy-in of all relevant stakeholders for effective implementation (including government funding) of surveillance and supporting programs.

Adequate funding to implement the plan

National insurance coverage for testing and treatment of HCC and its causes (i.e. hepatitis) to minimize out-of-pocket cost and maximize access to testing and treatment.

Robust surveillance protocols, education, precise and high quality treatments

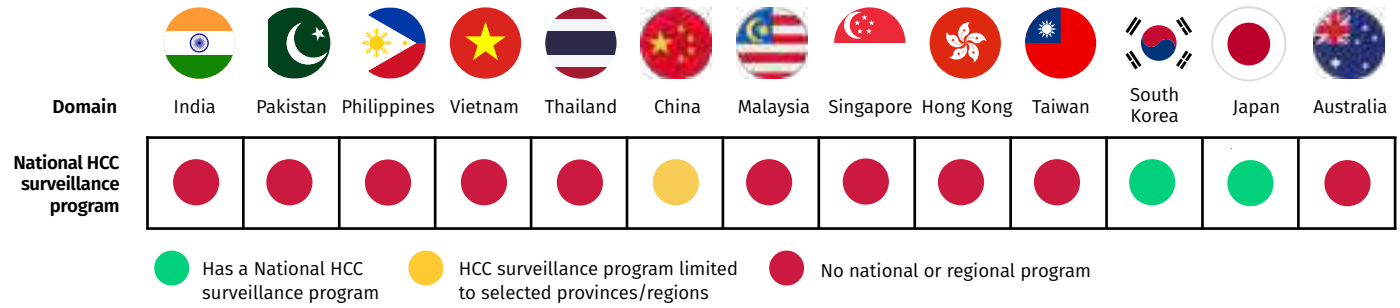
Ensures rigorous HCC surveillance is consistently applied across a target population that knows where, when and why to test for HCC, and HCC patients receive treatment that will maximize their chance of a cure (if detected early) or at least maximize survival.

Subsequently, we will examine different territory examples that highlight the successes and shortcomings in each of these four factors across the APAC region.

5.3.2 THE PRESENCE OF A NATIONAL HCC SURVEILLANCE PROGRAM

Among the 13 studied APAC territories, only Japan and South Korea have a national HCC surveillance program (see ***Figure 8***).

Figure 8: *Presence or absence of national HCC surveillance programs across APAC territories*



A national HCC surveillance program should aim to detect and manage HCC cases, especially among high-risk populations like viral hepatitis, cirrhosis, NAFLD/NASH, and metabolic syndrome[98].

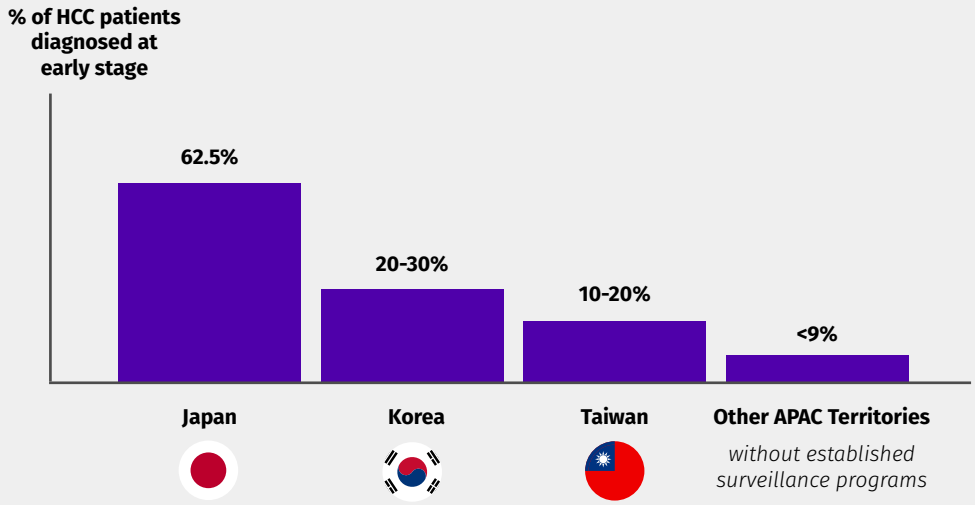
While fully reimbursing the program requires investment, it can incentivize participation and ensure equitable access[99,100]. Furthermore, implementing a nationwide program for HCC can be considered cost-effective and yield a positive return on investment, as explained in ***section 6*** of this paper. Partial reimbursement or exploring coverage through health insurance schemes can be alternative options[99,100]. Striking the right balance between financial considerations and access to necessary services is essential for an effective and sustainable HCC surveillance program[99,100].

A national HCC surveillance program should aim to detect and manage HCC cases, especially among high-risk populations like viral hepatitis, cirrhosis, NAFLD/NASH, and metabolic syndrome

Across healthcare systems in Asia, there exists significant variation in the overall survival rates of patients diagnosed with HCC[101]. Notably, Japan stands out with an impressive 5-year survival rate of 44.1% for all HCC cases, surpassing the rates reported in other countries globally during the same time frame[37]. For instance, South Korea recorded a survival rate of 23.3%, Taiwan reported 22%, and the United States demonstrated survival rates ranging from 11% to 15%[37]. Key factors that prolong long-term survival are early diagnosis of tumours, and treatment of patients with effective therapies[102,103].

NATIONAL SURVEILLANCE PROGRAM IS ASSOCIATED WITH EARLIER DETECTION OF HCC AND LONGER SURVIVAL

National surveillance programs lead to earlier detection of HCC, resulting in more patients being diagnosed at curable early stages (BCLC 0 or A). For example, in Japan, 62.5% of HCC patients are diagnosed at early stages, compared to 20-30% in South Korea, 10-20% in Taiwan, and <10% in other Asian territories without established surveillance programs[37].

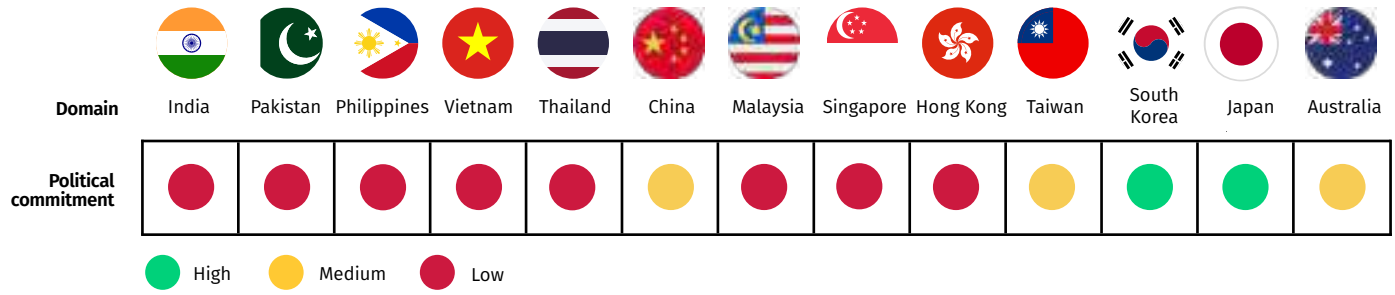


Studies have also shown that patients who undergo surveillance have better survival outcomes, where the median survival of HCC patients in Japan is 79.6 months, longer than other regions[37]. Similar improvements have been observed in South Korea, where the mortality risk of patients who participated in the surveillance program was 22.0% lower compared to those who did not[104].

5.3.3 SUFFICIENT POLITICAL WILL AND COORDINATION

Political will and commitment (see ***Figure 9***) are assessed based on the extent of institutional commitment represented by the presence (or absence of) national organization or task force to oversee or manage the planning and implementation of HCC surveillance efforts in each territory and government support for policies, partnerships or clinical research to control HCC in the past 2 years.

Figure 9: *Level of political commitment to comprehensive HCC management across 13 APAC territories*



The governments in Japan and South Korea were driven to implement national HCC surveillance programs after a sharp increase in mortality rates and the realization that HCC was the leading cause of premature mortality respectively[105–107].

The Japan Society of Hepatology (JSH) also lobbied the Ministry of Health, Labour, and Welfare (MHLW) for HCC surveillance of high-risk patients (i.e. patients with chronic viral hepatitis and cirrhosis)[105].

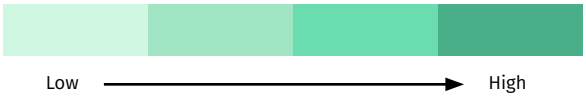
The coordinated efforts of the Japanese government, MHLW, academic societies, and government agencies have led to a system of free HBV and HCV testing in medical institutions and public health centers, including annual corporate and community health checkup programs[36,37]. These ultimately helped to detect patients at high risk of developing HCC early.

In contrast, other territories tend to overlook HCC and focus on cancers considered to have higher incidence and mortality, such as lung and breast cancer. However, Taiwan, Thailand, and Vietnam have not prioritized HCC surveillance despite the high incidence and mortality associated with HCC in each territory (see ***Table 2***). This underscores the need for increased attention and funding for HCC in these territories.

Table 2: *Incidence and prevalence of HCC by territory*[108–110]

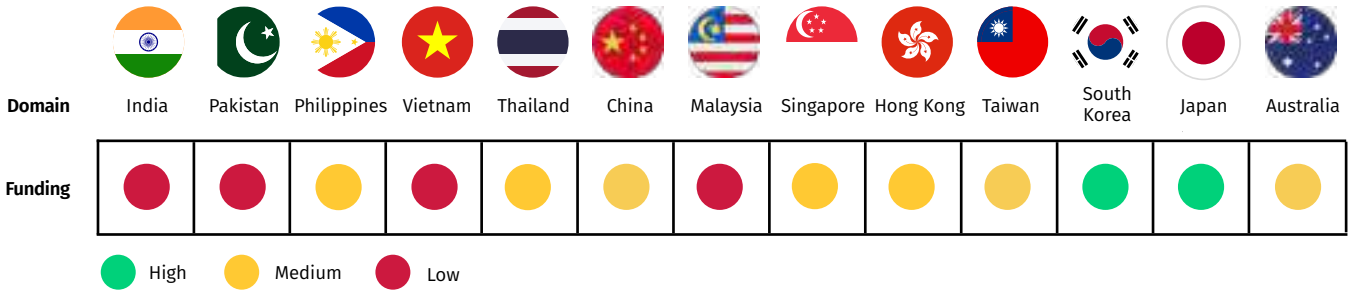
Territories	**Incidence** (crude rate per 100,000)	**Rank** 1 = Most common cancer	**Mortality** (crude rate per 100,000)	**Rank** 1 = Cancer with highest mortality
Singapore	23.0	6	21.7	4
China	28.3	5	27.0	2
India	2.5	11	2.4	11
Thailand	39.2	2	38.3	1
Vietnam	27.1	2	26.0	1
Japan	36.1	6	22.3	6
Republic of Korea	28.8	7	21.8	2
Philippines	11.6	7	10.7	4
Malaysia	6.6	9	6.3	5
Taiwan	47.8	6	33.3	2
Australia	11.6	7	10.7	4
Pakistan	2.4	13	2.3	10
Hong Kong	23.2	5	20.5	3

Colour legend



5.3.4 ADEQUATE FUNDING TO IMPLEMENT THE PROGRAM

Figure 10: *Funding for comprehensive HCC management across 13 APAC territories*



Adequate funding is crucial for the successful implementation of comprehensive HCC surveillance programs utilizing ultrasound and tumour markers (AFP, AFP-L3, and PIVKAII)[37]. Due to the limited availability and ability to detect early-stage HCC, the use of tumor markers holds significant importance[111,112]. Tumor markers supplement the existing diagnostic methods by providing additional value in identifying HCC at its initial stages to improve surveillance and testing uptake[111,112].

Japan is the only territory in our analysis that reimburses ultrasound and 3 tumour marker tests for HCC surveillance[105] (see ***Figure 10*** above). In contrast, the other territories either do not reimburse HCC surveillance testing at all, or only reimburse ultrasound for HCC surveillance. Even then, funding for surveillance tests alone is not enough – it is also crucial to provide hepatologists' or ultrasound technologists' (sonographers trained by hepatologists) training to develop their skills and expertise for more accurate detection of tumours with ultrasound. Japan stands out for the skill and expertise of their hepatologists and ultrasound technologists which allows them to detect tumours smaller than radiologists elsewhere and this is testament to their investment in this area[113].

Japan is the only territory in our analysis that reimburses ultrasound and 3 tumour marker tests for HCC surveillance

Recognizing the crucial need for adequate funding to support biomarker testing and enhance training programs for ultrasound technologists, it is equally important to emphasize the participation of primary care providers in managing these conditions. Their involvement can significantly contribute to the continuity of care. Hence, it is imperative to invest in fostering better coordination among primary, secondary, and tertiary healthcare centers. These measures aim to strengthen the healthcare system's response to liver disease and HCC, ultimately leading to improved patient outcomes and comprehensive care delivery.

The availability of reimbursed treatment is also essential to drive doctors' recommendation for surveillance and acceptance among patients. Without access to affordable treatment, surveillance uptake may be hindered as timely HCC treatment is the ultimate objective of surveillance.

The primary treatment for early-stage HCC is surgical resection[114]. In order to assess the effectiveness of a comprehensive HCC surveillance program aimed at detecting early-stage HCC, it is crucial to consider the quality and accessibility of HCC surgery, as well as its reimbursement. When it comes to advanced HCC treatment, it is necessary to evaluate the reimbursement status of immunotherapy. Among the 13 territories in our analysis, only Japan, Australia, China, Hong Kong, South Korea and Singapore reimbursed immunotherapies for HCC and this served as an indicator of willingness to fund/reimburse novel therapies for HCC.

It will thus be crucial to adopt a programmatic approach to funding and management of HCC in territories that do not follow a Fee for Service Scheme (like Japan)

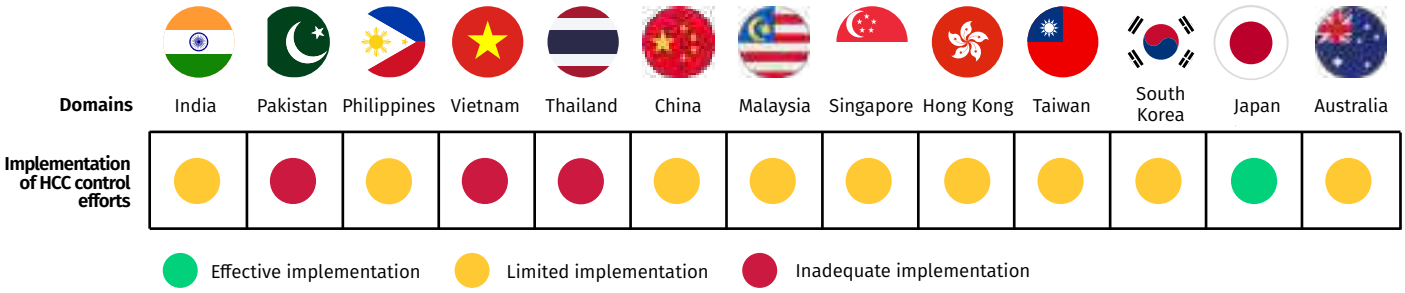
However, funding may remain a challenge in some territories even if HCC surveillance testing and treatment are reimbursed, especially in territories that do not follow a Fee for Service Scheme (like Japan). For instance, budget constraints from payors may keep the adoption and utilization of surveillance low. It will thus be crucial to adopt a programmatic approach to funding and management of HCC in these territories.

An efficient HCC surveillance program, which highlights the necessity and commitment to surveillance, eventually hinges on the effectiveness of the surveillance tests, characterized by high sensitivity and specificity. Moreover, the presence of an acceptable and effective therapy is crucial, as it ultimately leads to increased support and funding.

We will explore this in our key policy recommendations later in this white paper.

5.3.5 EXTENSIVE SURVEILLANCE PROTOCOLS, PUBLIC EDUCATION, CAREFUL AND ACCURATE TREATMENT SELECTION AND HIGH-QUALITY TREATMENT TECHNIQUES

Figure 11: *Implementation of HCC control efforts across 13 APAC territories*



While a combination of the AFP test and ultrasound is considered the gold standard for HCC surveillance by major international societies such as the American Association for the Study of Liver Disease (AASLD), the European Association for the Study of the Liver (EASL) and the Asian Pacific Association for the Study of the Liver (APASL) (with the exception of The Japan Society of Hepatology's clinical practice guideline which recommends ultrasound and 3 tumour markers – AFP, ALP-L3 and PIVKAII)[115,116], the sensitivity of AFP and ultrasound combination in detecting early stage HCC is suggested to be 60%[117] meaning that 40 out of 100 patients may not receive an early diagnosis despite undergoing surveillance. For this reason, up to 30 to 40% of tumours detected under surveillance are beyond early stage HCC[118]. The addition of complementary biomarkers (PIVKA and AFP-L3) to ultrasound and AFP has been suggested to further increase sensitivity and address this limitation[119].

Japan's comprehensive HCC surveillance approach with ultrasound and 3 tumour markers has paid off, with a higher proportion of early HCC detection and improved prognosis[37,105], thus supporting the increased sensitivity of ultrasound and 3 tumour markers over ultrasound and AFP alone.

There is also evidence that demonstrates the cost-effectiveness of combining ultrasound, AFP, ALP-L3 and PIVKAII over a combination of ultrasound and AFP[120] – we will discuss this in the next section.

Moreover, research has shown that genomic profiling can be utilized to detect HCC at an early stage in cirrhotic patients, thereby addressing the necessity of identifying HCC cases that can benefit from curative treatments. Given its remarkable precision, non-invasive nature, and applicability across diverse populations, genomic profiling holds immense potential for public health screening among high-risk groups, particularly in situations where the essential equipment and infrastructure for HCC imaging screening are unavailable, although there is a need to consider affordability.

Earlier we discussed the importance of funding for surveillance, but this also needs to be accompanied by education initiatives to drive testing uptake.

If testing costs do not pose a barrier to patients, awareness and knowledge of testing become the key determinant of surveillance uptake[121]. The suboptimal surveillance uptake in South Korea has been attributed to a lack of patient awareness and knowledge of the need for HCC surveillance[122].

Besides its nationwide surveillance program, the better survival outcomes reported in Japan can also be attributed to its accurate diagnostic imaging capabilities, and technical superiority of resection and locoregional therapies including RFA and superselective conventional TACE[37,123] as well as proactive introduction of systemic therapy including molecular targeted therapy and immunotherapy for not only advanced stage but also for intermediate-stage HCCs. Japan's superior outcomes in BCLC stage A HCC can attributed to the stringent assessment of hepatic functional reserve and proactively repeated resections in resectable cases[37,123]. In addition, Japan has unique treatment approaches for HCC patients with vascular invasion, such as HAIC, that have shown beneficial effects in selected HCC patients with vascular invasion and were reported to have a better prognosis than those treated with other therapies[37].

06 The investment case for hepatitis elimination and HCC management

We examined cost-effectiveness (i.e. health gains relative to the cost of the intervention)[124] and cost-benefit (i.e. cost of the intervention relative to the benefits of the intervention, where benefits include health outcomes and non-health benefits such as productivity gains, quality of life, etc)[125] data to assess the value of various interventions for hepatitis and HCC in APAC.

These interventions ranged from one-time screening to comprehensive elimination programs. Cost-effectiveness and cost-benefit data were not available in all 13 APAC territories so we focused on a sub-set of territories (Australia, Japan, China, South Korea, Pakistan, Vietnam, Philippines) to represent the income spectrum in the region. Our analysis showed that HBV and HCV treatment, screening, and comprehensive elimination packages are cost-effective as they fall below the cost-effectiveness threshold of USD25,000 per quality-adjusted life-years (QALY) gained set by NICE[126] or below a threshold of USD998 (in territories with low human development index / HDI like Pakistan) to USD69,499 (in territories with very high HDI like Australia) per disability-adjusted life year (DALY) averted[127]. For HCC surveillance, biannual ultrasound combined with AFP was the most cost-effective option for high-risk patients with cirrhosis and chronic HBV.

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6.1 THE INVESTMENT CASE FOR HEPATITIS B ELIMINATION

Cost-effectiveness and cost-benefit data highlighted the urgency and value of eliminating HBV in Australia, China, Philippines and Vietnam.

A five-test (HBsAg/HBsAb/HBeAg/HBeAb/HBcAb) screening strategy was shown to be the most cost-effective in China with incremental cost-effectiveness ratio (ICER) of USD18,295 per QALY gained[128].

The cost-effectiveness of the five-test screening strategy can be attributed to the marginal cost increase per test as compared with other strategies (e.g. the five-test strategy has a marginal cost increase of USD8.55 per test compared with the two-test strategy)[128]. The youngest age group (18-30 years) would also benefit most from screening because identifying younger people who need vaccination would result in greater QALYs gained from a fixed investment sum. This underscores the urgency to screen for HBV.

A comprehensive HBV elimination program consisting of diagnosis, linkage to care, treatment and prevention/vaccination has also been shown to be cost-effective and saves health system resources. A study assessing the cost-effectiveness of scaling up HBV diagnosis, linkage to care and treatment (i.e. enhancing the HBV care cascade) to achieve WHO's HBV elimination targets in Australia by 2030 found that this had an ICER of USD9,735 per DALY averted[129]. Likewise, a full suite of prevention (100% infant vaccination and prevention of mother-to-child transmission), case finding and treatment (50% coverage) in China would avert 2.1 million HBV-related deaths and yield a return of USD1.57 per USD1 dollar invested over a span of 15 years[130]. Similarly, every USD1 dollar spent on HBV elimination in Philippines and Vietnam will return USD2.23 and USD1.70 respectively by 2035[131].

6.2 THE INVESTMENT CASE FOR HEPATITIS C ELIMINATION

Similarly, cost-effectiveness and cost-benefit data highlighted the urgency and value of eliminating HCV in Australia, China, Pakistan and Vietnam. HCV screening can yield an ICER of USD104 to USD2,647 per person diagnosed in Vietnam and China respectively[132]. Combining screening with treatment will lead to an ICER of USD2,030 to USD4,956 per person cured in Vietnam and China respectively[132].

HCV screening and treatment have been shown to be cost effective

HCV Screening	Treatment	ICER Generated per QALY (USD) Vietnam	ICER Generated per QALY (USD) China
✗ / ✓	✗ / ✗	104	2,647
✓ / ✓	✗ / ✓	2,030	4,956

A modelling study assessing the cost-effectiveness and net economic benefit of scaling up hepatitis elimination with testing and treatment in Australia concluded that investing an additional USD163 million to achieve WHO HCV elimination targets by 2030 will yield an additional net economic benefit of USD183 million and this benefit would continue to increase every year thereafter[17].

Likewise, another study concluded that investment in HCV elimination in Pakistan can bring about substantial societal health and economic benefits[133]. Scaling up screening and treatment to achieve HCV elimination in Pakistan could avert 5.57 million DALYs and 333,000 HCV-related deaths from 2018 to 2030[133]. This elimination initiative could cost an additional USD1.45 billion in direct costs if one-third of HCV screening were integrated within existing primary healthcare services in Pakistan. However, USD1.30 billion could be saved over the same period through improvements in productivity from reduced absenteeism, presenteeism, and premature deaths due to HCV. This would make the investment highly cost-effective (ICER: US$29 per DALY averted) by 2030 and cost-saving shortly after, with a net economic benefit of US$9.10 billion by 2050[133].

Scaling up screening and treatment could avert

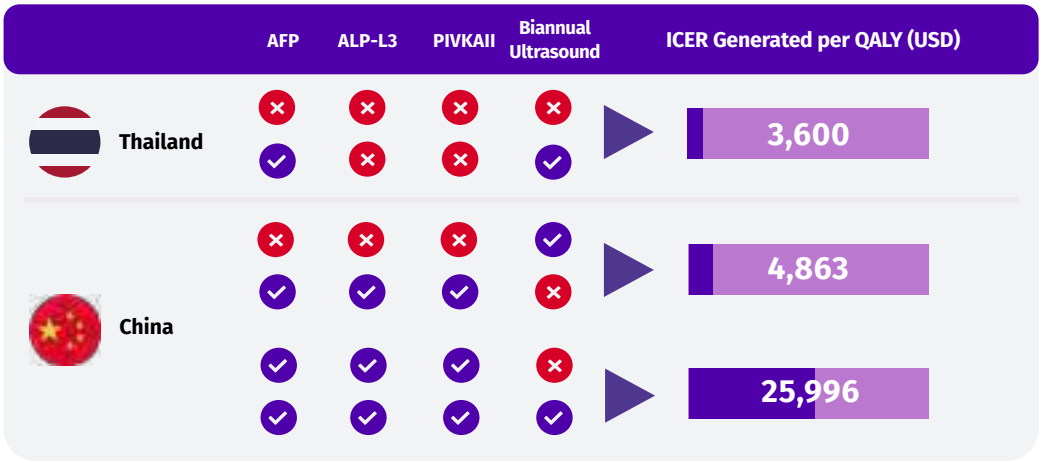
- **5.57 million DALYs**
- **333,000 HCV-related deaths**

6.3 THE INVESTMENT CASE FOR HCC SURVEILLANCE

In general, surveillance is considered beneficial to an individual if it provides an increase in life expectancy of around 100 days, and cost-effective if surveillance costs less than USD50,000 per year of life gained[134]. A systematic review revealed that biannual ultrasound and AFP stand out as the most cost-effective surveillance method across Australia, Thailand, South Korea, which is in line with recommendations from Asia-Pacific and Australian professional bodies for patients with cirrhosis and chronic HBV[135]. This combination improves screening sensitivity (despite the trade-off regarding decreased specificity) and is also more cost-effective than ultrasound alone. For instance, biannual ultrasound ± AFP was cost-effective when compared with no screening in Thailand, with an ICER of USD3,600/QALY[135], thus meeting the criteria for surveillance to be considered cost-effective. However, this systematic review did not consider the benefit of combining ultrasound, AFP, ALP-L3 and PIVKAII over ultrasound and AFP.

Another cost-effectiveness analysis of serological tests and ultrasound revealed that combining ultrasound, AFP, ALP-L3 and PIVKAII is the most cost-effective strategy among chronic HBV patients over 40 years of age in China[120]. The ICER of the AFP, ALP-L3 and PIVKAII combination over ultrasound alone was USD4,863 per QALY while the ICER of the AFP, ALP-L3 and PIVKAII combination over a combination of AFP, ALP-L3, PIVKAII and ultrasound was USD25,996 per QALY[120]. Once again, this met the criteria for surveillance to be considered cost-effective.

HCC surveillance that combines ultrasound and multiple serological tests is cost effective



Surveillance is considered cost-effective if it costs **<USD 50,000** per year of life gained.

An examination of cost of illness (COI) which is calculated by summing direct, morbidity and mortality costs, suggested the economic burden of HCC is lower in Japan than Taiwan[136]. In Japan, COI trended downwards and COI in 2014 was 33% lower than COI in 2002 while COI trended upwards in Taiwan with COI in 2014 being 16% higher than that in 2002[136]. Loss of human capital due to death caused by HCC was the largest contributor to COI[136]. This suggests that the lower (and downward trending) COI in Japan could be attributed to the national surveillance program which has led to earlier diagnosis and improved prognosis of HCC patients and demonstrates the cost-effectiveness of nation-wide HCC surveillance.

Comparing COI between 2002 and 2014

-33% COI trended **downwards** *with surveillance program*

+15% COI trended **upwards** *without surveillance program*

07 Key policy recommendations for HBV, HCV and HCC

While progress has been made in many of the APAC territories, intensive work still lies ahead to reach the goal of eliminating hepatitis and reducing the economic loss associated with HCC. In this section, we lay out five action points, which present our policy recommendations for APAC's response to hepatitis and HCC. These action points are exemplified through successful case studies within individual territories in the region and one from Egypt, providing learnings for all territories. Additionally, the action points have also been formulated by considering the lessons and shortcomings observed in other regions, such as Australia.

The case studies also underscore the benefits of coordinating a national healthcare response to both hepatitis and HCC, in contrast to the siloed approach adopted by many territories in the APAC region[36].

The above-mentioned policy recommendations embody this coordinated response and will ultimately benefit all stakeholders in the healthcare ecosystem. The value of these interventions have been summarized on the next page before we deep dive into the 5 action points in the rest of this section.

FIVE ACTION POINTS TO ELIMINATE HEPATITIS AND CONTROL HCC

1. HEPATITIS NATIONAL ACTION PLANS NEED TO BE MORE COMPREHENSIVE
2. EXPAND HEPATITIS SCREENING AND TREATMENT, INTEGRATED WITHIN EXISTING HEALTH SYSTEMS AND TAILORED TO THE NEEDS OF AFFECTED POPULATIONS IN VARIOUS SETTINGS
3. GOVERNMENTS CAN SECURE GREATER FUNDING BY INTEGRATING HEPATITIS AND HCC INTO BROADER HEALTH INITIATIVES AND EMPLOYING BLENDED FINANCING MODELS
4. IMPLEMENT A COMPREHENSIVE NATIONAL HCC SURVEILLANCE PROGRAM AND ENSURE TIMELY ACCESS TO TREATMENT FOR HCC AND HEPATITIS
5. INCREASE AWARENESS AND IDENTIFY POLICY CHAMPIONS TO DRIVE POLITICAL COMMITMENT

VALUE OF STRONG HEPATITIS ELIMINATION AND HCC SURVEILLANCE PROGRAMS

Patients and their caregivers:

- De-stigmatization
- Improved access to screening, surveillance and treatment
- Chance of curing HCV
- Better prognosis for HBV and HCC

Healthcare professionals:

- Timely and appropriate clinical response
- Confidence in screening and diagnostic results

Governments and the economy:

- Healthier population a better economic productivity
- Reduce absenteeism due to debilitating symptoms associated with chronic HBV and late-stage HCC

Healthcare systems and payors:

- Progress towards UHC
- Increase cost-effectiveness by detecting and treating early
- Enhance economic efficiencies by adding hepatitis screening (and HCC surveillance) to existing health services such as TB, HIV
- Generate cost-effectiveness data using micro-elimination

Healthcare providers:

- Reduce operational costs and set-up time by combining hepatitis screening with other health services for TB/HIV
- Alleviate bed crunch by detecting and treating patients early before progression to chronic HBV and HCC

7.1 ACTION POINT 1: Hepatitis national action plans need to be more comprehensive

Japan and Taiwan's experiences demonstrate the positive outcomes of effective policy communication and coordination efforts, coupled with a forward-thinking perspective that ensures sustainable financing[136]. The case study of Taiwan is detailed in ***Boxes 2*** and ***3***.

Hepatitis national action plans should also incorporate WHO hepatitis elimination targets outlined in the WHO Global Health Sector Strategy (GHSS) on viral hepatitis released in 2016, as this provides an initial roadmap for the elimination of viral hepatitis as a public health problem by 2030 – a 90% reduction in incidence and a 65% reduction in mortality by 2030, compared with a 2015 baseline[18].

The subsequent release of the first-ever WHO Global Guidance for country validation of viral hepatitis elimination in 2021 has marked a significant milestone in the field and represents a major step forward in the fight against viral hepatitis. It has quickly established itself as a valuable and comprehensive resource to support territories' viral hepatitis elimination efforts. This Guidance accounts for territory variances in HBV and HCV epidemiology and progress toward elimination, thus giving territories the flexibility to adapt its recommendation to the local context[18]. For instance, territories can apply separately for one of four certification options: elimination of mother-to-child transmission of HBV, HCV as a public health problem, HBV as a public health problem, or elimination of both HBV and HCV together as a public health problem. This flexible approach recognizes the diverse challenges and priorities that territories may face, including both low-middle income and high-income territories, enabling them to tailor their elimination strategies based on their unique circumstances and resources. The Guidance also provides a range of options for how to measure the targets depending on available surveillance data and capacity, as well as a checklist of other considerations to assess their progress towards elimination[18].

Encouragingly, some countries have also integrated their broader healthcare objectives with the WHO's 2030 elimination goal, extending beyond hepatitis-specific plans. A notable example is China's Healthy China 2030 plan that includes targets for HBV elimination by 2030.

Through health-care system reform and enhanced professional training, the Chinese government can revitalize the delivery of HBV-related services, ensuring a robust service framework towards achieving the elimination goal by 2030[137].

Besides the WHO guidance, there are also other publicly available resources, such as the Coalition for Global Hepatitis Elimination (CGHE)'s Hepatitis C (HCV) Elimination Tool, which can support territories in budget-based planning and the development of national strategies for HCV elimination.

BOX 2: TAIWAN CASE STUDY
Taiwan is on track to eliminate HCV by 2025[72]

Before 2018, there was a lack of large-scale screening programs for HCV and there was sub-optimal treatment coverage of 20%-30% despite the high disease burden of HCV in Taiwan.

In 2018, Taiwan committed itself to achieving WHO's 2030 goal of treating 80% of eligible patients by 2025. This commitment is underscored by the Taiwan Hepatitis C Policy Guideline 2018-2025 which demonstrated political commitment by MOHW to eliminate HCV through active screening and relaxation of treatment reimbursement criteria whilst ensuring sustainable financing.

This policy guideline identified 3 policy directions:
1. therapy spear-heading prevention
2. screening supports therapy
3. prevention securing outcomes

These are in turn underpinned by 3 strategies:
1. precision public health approach for screening
2. patient-centered continuum of care spanning prevention to follow up
3. localized care delivery to increase access and equitable care to even remote regions

A special budget (NTD20.8 billion or USD680 million) was set aside to treat 120,000 patients with curative DAA in 2017-2020, corresponding to 30% treatment coverage. As of 2021, restrictions on DAA treatment have been gradually lifted so all HCV patients, regardless of chronicity, could access DAA.

Universal HCV screening with anti-HCV and HBsAg was also implemented in 2020 for adults older than 45 years old.

Linkage to care was ensured by (1) linking prevention, screening, diagnosis and treatment with case management and information platform; (2) tailoring prevention and control strategies based on prevalence, geographical accessibility and special populations (e.g. sex workers, MSM, drug needle users); (3) localized care delivery.

Following the launch of this policy, the number of patients with HCV infection treated annually has increased almost 5-fold across 2 years, rising from 9,500 patients in 2017 to 46,000 in 2019. As of Aug 2022, 142,718 HCV patients have been treated with DAA and Taiwan is on track to achieve its goal of treating 250,000 HCV patients by 2025.

BOX 3: TAIWAN CASE STUDY
Taiwan has made great strides in HBV vaccination, treatment and monitoring[138].

The Viral Hepatitis Control Program (VHCP) in Taiwan played a very important role in the prevention and control of HBV infection. Each stage of the VHCP has had a different focus; universal vaccination being the focus in the early stages of the VHCP and the provision of treatment for chronic viral hepatitis B and C being the aim since 2003.

Universal vaccination

Taiwan recognized that mother-to-infant transmission of HBV resulted in a high rate of chronic HBsAg carriage, and is a major route of HBV transmission. Thus, the most effective way to prevent new HBV infections is to interrupt the virus infection early in life.

A mass vaccination program (overseen by the Ministry of Health and Welfare) was thus launched in 1984. It initially targeted at the newborns of hepatitis B carrier mothers and later extending to all newborns in 1986. The coverage rate of vaccination in newborns has generally been >95% for the last 30 years, and recently reached 98%. Vaccination has also been shown to reduce complications of HBV such as HCC - the incidence of HCC in children 6–9 years of age decreased from 0.52 per 100,000 children in those born before the vaccination program to 0.13 per 100,000 in those born after the program.

HBV treatment provision

Despite the success of the vaccination program in the younger generation, the prevalence of HBV infection in the adult population before the era of universal vaccination remains high, with >90% of the adult population greater than 35 years of age having been infected with HBV and 12–15% of them remaining HBsAg positive.

To that end, patients with known chronic HBV infection but without active anti-HBV treatment are followed up at local clinics or hospitals every 6 to 12 months. Liver function tests, alpha-fetoprotein, and abdominal ultrasonography are performed regularly. Subjects without a history of viral hepatitis infection have been able to receive free tests for hepatitis B virus (HBsAg) and hepatitis C virus (anti-HCV) infection at the age of 45 years since 2011.

Today, the national health insurance covers all costs related to outpatient visits, laboratory monitoring, and the drug itself for chronic HBV patients. The costs of both IFN and NUCs are now reimbursed for the treatment of chronic HBV in Taiwan.

As a result, the proportion of HBV-related HCC has decreased gradually over the last 20 years in Taiwan. In 2001, the percentage of HCC attributable to HBV infection was 66% in male patients and 41% in female patients. In 2015, the overall percentage of HBV-related HCC further decreased to 40%.

7.2 ACTION POINT 2:
Expand hepatitis screening and treatment, integrated within existing health systems and tailored to the needs of affected populations in different settings

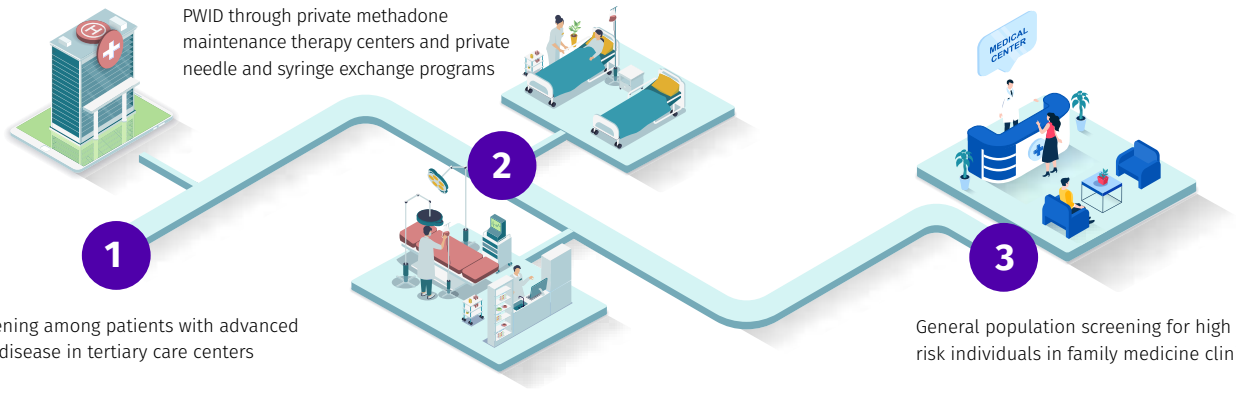
We have identified three types of hepatitis screening programs based on the stepwise approach to designing a national hepatitis screening strategy and experiences of the 13 APAC territories analyzed in this white paper:

1. Opportunistic screening among patients with advanced liver disease in tertiary care centers
2. Micro-elimination screening programs targeting high risk populations such as PWID or PLHIV (for HCV) or pregnant women (for HBV) in the community or primary care setting
3. General population screening program at a provincial or national level where screening candidates would be identified at primary, community, district or tertiary health settings based on high risk behaviours or profiles

A stepwise approach to designing a national HCV screening strategy was used in Malaysia – this began with opportunistic screening among patients with advanced liver disease in tertiary care centers before progressing to PWID through private methadone maintenance therapy centers and private needle and syringe exchange programs and finally general population screening for high risk individuals in family medicine clinics[139]. This stepwise approach can serve as a roadmap for territories without a national screening program to progress from current opportunistic/provincial/micro-elimination screening programs to a national general population screening program. This would allow policymakers and program planners to identify a window period to develop the operational capacity for a national general population screening program[139].

The stepwise approach was also shown to be 40% less costly than a strategy that immediately adopted widespread general population screening in Malaysia[139].

STEPWISE APPROACH TO DESIGNING A NATIONAL HEPATITIS SCREENING STRATEGY



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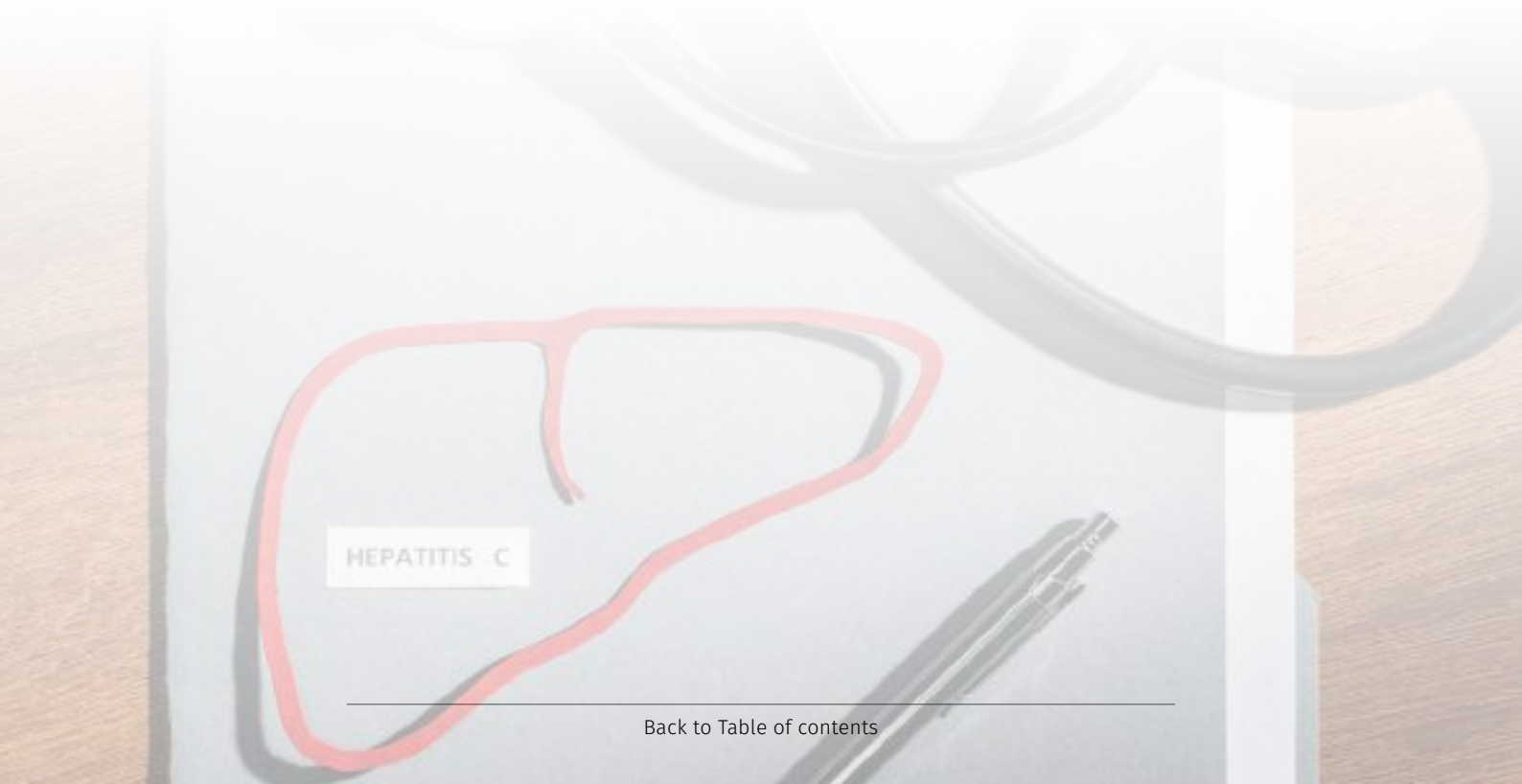
Crucially, a sensitivity analysis of the stepwise approach in Malaysia also highlighted the importance of linkage to care. If linkage to care for high risk or general population dropped 5% below baseline, the WHO elimination target would not be achieved by 2030[139]. Conversely, if linkage to care proportions increased by 5% above baseline, then the screening program would become less costly[139]. Australia's experience (see ***Box 4***) also highlights the importance of linkage to care to achieve the goal of eliminating hepatitis C virus (HCV) by 2030.

Looking ahead, it will also be important to broaden the scope of hepatitis screening to eliminate hepatitis and control HCC effectively. Approximately 13% of individuals who test positive for HBsAg are coinfected with HDV[140]. This coinfection has synergistic effects on the severity of liver disease, leading to an increased risk of cirrhosis and a higher incidence of HCC compared to chronic HBV alone[140].

BOX 4: AUSTRALIA CASE STUDY
Strengthening linkage of care to eliminate HCV by 2030[81,141]

As mentioned above, HCV elimination programs in Australia need to maintain treatment uptake by focusing on increasing testing and linkage to care. This is crucial given that most patients currently on HCV treatment had been diagnosed for some time; people with newly acquired infections need to be linked to treatment to ensure that they do not drop out. Patient navigation or care coordination and integration of HCV care into drug treatment settings will help to strengthen linkage to care for people with newly acquired infections who tend to be people who inject drugs.

It will also be important to consider the implementation of evidence-based interventions that have been shown to enhance HCV testing, including medical chart reminders, dried-blood-spot testing, point-of-care HCV antibody testing, point-of-care HCV RNA testing, and reflex HCV RNA testing. This will allow Australia to scale-up testing and early detection of people with newly acquired infections, especially so given their marginalized status.



Hepatitis and HCC screening, diagnosis, and treatment may not always be readily available to those in need, especially at the primary care setting. However, primary healthcare settings are often overburdened, and therefore targeted services and programs need to be tailored to different settings. This may include centralized testing and treatment in urban and suburban areas, and decentralized testing and treatment in rural and remote areas to increase access.

For example, Egypt's success in scaling up HCV screening can be attributed in part to private-public partnerships with diagnostics partners which supported local teams with installation and training, and made agreements with third-party logistics companies to provide mobile testing facilities[142].

Another angle we can consider is Taiwan's efforts in improving the HCV care cascade, more specifically by increasing HCV diagnostics rate and treatment uptake, via HCV reflex testing. Traditionally, HCV is diagnosed using a 2-step process, where anti-HCV testing is conducted first, followed with HCV RNA test for individuals who are anti-HCV seropositive. Due to the multistep process, it seems to prevent individuals from seeking timely HCV care. With reflex HCV testing however, the HCV care pathway is simplified, and time taken in between stages is effectively reduced. Therefore, it has the potential to bridge gaps between diagnosis and treatment. This is evident from the near 3-fold improvement in treatment rate after reflex HCV testing was implemented[143]. Furthermore, to further encourage more countries to bridge this gap, WHO has updated its guidelines last year to incorporate reflex HCV testing as an additional diagnostic to promote linkage to care[144].

Hepatitis initiatives can also be added to existing health systems or health initiatives, such as HIV and TB testing and treatment services (for HCV and HBV), maternal and child health clinics (for HBV) or harm reduction and drug dependence treatment services (for HCV). Meaningful partnerships with communities affected by HIV and TB could also be replicated for viral hepatitis to enhance the impact of response design and delivery[33]. This can be part of horizontal health programs that leverage existing infrastructure and reach among hard-to-reach or marginalized populations. The programmatic synergies also extend to monitoring and evaluation where the global monitoring and evaluation framework for HBV is similar to HIV while that for HCV is similar to TB[33].

The above-mentioned combinations require close collaboration among different stakeholders who traditionally plan and execute programs for different diseases, and the creation of a national task force, as seen in examples like Taiwan's National Hepatitis C Program (NHCP) office and Egypt's National Committee for the Control of Viral Hepatitis (NCCVH), which can facilitate coordination efforts and have been cited as critical success factors.

7.3 ACTION POINT 3: Governments can secure greater funding by integrating hepatitis and HCC into broader health initiatives and employing blended financing models

To secure greater catalytic funding and sustainable domestic funding for hepatitis and hepatocellular carcinoma (HCC) programs, it is essential to integrate them into broader health initiatives[147]. Currently, catalytic external funding for hepatitis in APAC is predominantly limited to key populations at risk of HIV, with funding from organizations such as The Global Fund only available if hepatitis interventions target key populations at risk of HIV[147].

7.3.1 GLOBAL FUNDERS CAN CATALYZE GOVERNMENT INVESTMENT TO ELIMINATE HEPATITIS, SAVE LIVES AND GENERATE A NET ECONOMIC BENEFIT

Catalytic external funding can play a crucial role in generating cost-effectiveness evidence, which is often a pain point in research, to convince governments to allocate domestic funding for hepatitis and HCC programs[89]. For instance, in Cambodia, external funding contributed to the government's decision to eventually fund and launch a national hepatitis program[148]. CHAI has also published a Hepatitis Resource Toolkit to help countries navigate The Global Fund 2023 funding application process[87]. The Toolkit equips a wide range of stakeholders such as ministries of health, partners, and civil society, with the information and tools to understand The Global Fund's hepatitis-related policies and processes to develop strong proposals for the 2023-2025 funding round[87].

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Micro-elimination strategies can also demonstrate cost-effectiveness in smaller patient sub-groups, generating buy-in for increased domestic funding of hepatitis and HCC programs for other patient groups or the general population.

Taiwan serves as an example where micro-elimination in dual HIV+HCV infected patients and incarcerated persons showed early success and generated momentum for comprehensive elimination[72]. A special budget of NTD 20.8 billion (~USD 680 million) was allocated to treat 120,000 patients with DAA from 2017 to 2020, corresponding to 30% treatment coverage. As of 2021, restrictions on DAA treatment have been gradually lifted, allowing all HCV patients, regardless of chronicity, to access DAA treatment[72].

Egypt also provides an example of how territories can allocate external funding from organizations such as the World Bank to health programs like HCV elimination by integrating them within broader health initiatives (see ***Box 5***)[142]. By integrating hepatitis and HCC programs into broader health initiatives and leveraging catalytic funding, territories can secure greater funding opportunities and sustainable domestic funding for comprehensive and effective responses to these diseases[142]. As detailed earlier in this paper, such elimination initiatives can prevent up to 4.5 million deaths by 2030[19] and return up to USD2.23 per USD1 invested by 2035[131].

BOX 5: EGYPT CASE STUDY
Egypt received $530 million in funding from the World Bank as a result of prioritizing health resources for addressing HCV[142]

In 2016, the World Bank and the Egyptian government began collaborating on modelling scenarios for the elimination of HCV. The World Bank estimated that the more ambitious elimination scenario would be much more expensive in the short term, but the long-term benefits would be considerable – an estimated $420 million saved between 2023 and 2030. Most of these savings were forecast to come through preventing HCV-related complications such as liver cancer.

Based on these findings, and thanks to the development of cheaper treatments and screening tools, the government shifted from control to elimination and committed to providing care for free. The World Bank committed $530 million from the International Bank of Reconstruction and Development as part of a project that included the hepatitis elimination campaign, but also targeted broader efforts to strengthen primary and secondary care and enhance demand for health and family planning services.

A transferable insight for other territories is that the Egyptian government chose to prioritize health programming within the funds that it could borrow from a financing institution such as the World Bank and focused a large proportion of that funding on HCV elimination. Egypt could equally have not focused on health, but on infrastructure or other aspects of development. Resources may be available for similar projects in other territories if governments choose to prioritize health.

7.3.2 GOVERNMENTS SHOULD EMPLOY BLENDED FINANCING MODELS TO SECURE GREATER CATALYTIC FUNDING AND SUSTAINABLE DOMESTIC FUNDING

Blended financing is the strategic use of development funds, such as those from government aid and philanthropic sources, to catalyze and mobilize private capital for social and environment results[149]. Health-related blended financing solutions represent a mostly untapped tool in this regard as they currently account for only a fraction of the overall market[149].

Blended financing models have been employed successfully to augment domestic financing and sustain the scale up of hepatitis health programs

For example, China has rolled out a HBV catch-up vaccination program for 15 million children with support from the Global Alliance on Vaccine and Immunization, including an investment of USD76 million to subsidize the catch-up program through public-private partnerships such as with Rotary and the ZeShan Foundation[150]. There are also existing mega-funds set up through large international agencies building upon private-public initiatives such as initiatives for HIV/AIDS treatment provision. These HIV funding bodies may be interested in funding hepatitis treatments in hepatitis/HIV co-infected subjects, especially in territories where efficient HIV therapy has resulted in an increased quality of life for HIV patients, but who are now suffering more from HBV or HCV symptoms[151].

7.3.3 GOVERNMENTS NEED TO INVEST IN HEPATITIS ELIMINATION AND HCC SURVEILLANCE TO SAVE LIVES, AVERT ECONOMIC LOSS AND PROGRESS TOWARDS UHC

Framing funding for hepatitis and HCC programs as part of the wider effort to achieve universal health coverage can garner support for domestic funding. A programmatic approach to funding and management of HCC will be crucial to drive surveillance and treatment uptake especially in territories that do not follow a Fee for Service Scheme like Japan. For instance, a program budget should be set aside for a public health program that implements reimbursed national HCC surveillance to achieve universal health coverage for cancer patients (as per UN SDG No. 3[152]) and implementation of key indicators to track adoption and impact.

National health insurance can also be expanded to include outpatient care, and territories can implement less resource-intensive screening alternatives, such as blood-based biomarker testing, as an alternative to ultrasound for HCC screening.

These alternatives can also be integrated into existing programs like annual health checks for employees, rather than standalone programs which may be deemed a hassle. These approaches can help improve access to screening, diagnosis, and treatment for hepatitis and HCC, and reduce the burden of these diseases on healthcare systems and patients.

Organizations can also kick-start domestic funding discussions for hepatitis and HCC programs by integrating funding into existing programs or services for other diseases, such as HIV. Leveraging the well-established infrastructure and investment in HIV testing and treatment can bridge services/programs for hepatitis and prevent costly and fatal long-term complications like HCC. The COVID-19 pandemic has also led to investment and enhancement of healthcare infrastructure and capacity, which can be leveraged for hepatitis and HCC initiatives.

Given the political sensitivities associated with supporting PLHIV in certain territories, governments need to identify and develop their funding requests to expand the funding opportunities for initiatives that target other sub-populations (e.g. incarcerated persons, indigenous populations, pregnant mothers) or the general population.

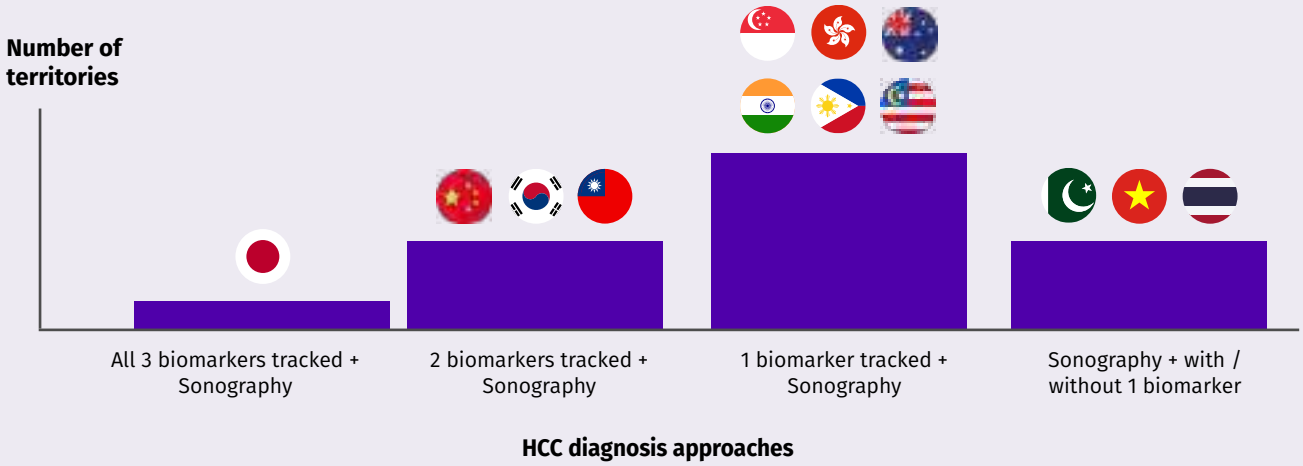
7.4 ACTION POINT 4:
Implement a comprehensive national HCC surveillance program and ensure timely access to treatment for HCC and hepatitis

Increasing the uptake of surveillance among at-risk populations has been shown to be more beneficial than incremental improvements to current surveillance methods

Japan's experience (detailed in ***Box 6***) and the Japan Society of Hepatology's clinical practice guideline provide a roadmap and framework respectively to mitigate the heavy clinical, economic, societal, and humanistic burden of HCC.

HCC surveillance can be optimized by implementing a national surveillance program that uses ultrasound and 3 tumour markers (AFP, PIVKA-II, AFP-L3) as exemplified by Japan's approach. However, as ***Figure 12*** below shows, most APAC territories only track 1 biomarker and do not have any national surveillance programs for HCC.

Figure 12: *No. of biomarkers tracked by each APAC territory*



3 biomarkers. AFK, PIVKAII, AFP-L3; 2 biomarkers. AFK & PIVKAII; 1 Biomarker. AFK

Note: Liver ultrasonography is a standard HCC surveillance test unanimously advocated by Asian guidelines. Apart from AFP, AFP-L3 and PIVKA11/DCP are also tumour markers used in clinical practice in Asian territories, especially Japan.

Increasing the uptake of surveillance among at-risk populations has been shown to be more beneficial than incremental improvements to current surveillance methods[153]. This serves as a crucial starting point, especially in territories where hepatitis B virus (HBV) is the primary cause of HCC or where there are limited resources. For instance, preventing mother-to-child HBV transmission will be crucial if there is a high prevalence of vertical or mother-to-child transmission of HBV infections[24]. Accurate risk stratification of patients is also needed to allow for targeted interventions, as availability of antiviral therapy can reduce the risks of HCC development and recurrence, but patients with advanced chronic liver disease remain at risk even after virological suppression or cure, and therefore require ongoing surveillance[154]. Individuals can also leverage data and technology to better risk stratify patients, such as developing risk assessment algorithms that allow providers to identify high-risk patients and recommend surveillance appropriately.

Ultimately, a national HCC surveillance program should aim to detect and manage HCC cases at early stages, especially among high-risk populations like viral hepatitis, cirrhosis, NAFLD/NASH, and metabolic syndrome[98]. The stage at cancer diagnosis is the primary determinant of overall survival in patients with HCC as early-stage diagnosis allows patients to receive curative treatments such as resection, ablation, or liver transplantation, resulting in significantly better long-term survival rates[115]. An observation registry study that evaluated differences in patient characteristics and treatment outcomes in 39 countries across five global regions including Asia Pacific noted that HCC patients in Japan were diagnosed at earlier stages and had a considerably longer survival time from diagnosis as compared with patients in Europe, USA and other Asian countries, potentially due to the national HCC surveillance system in Japan[123]. This longer survival was also observed across cancer stages, indicating that other medical factors in addition to early diagnosis contributed to this improved outcome[123]. This underscores the need to improve early detection and treatment in other regions including Asia Pacific[123].

Building upon the importance of surveillance, the inclusion of HCC within the National Cancer Control Plan serves as a crucial step. This strategic move highlights the significance of HCC as a national priority, emphasizing the need for a comprehensive approach to address it.

Following this integration, territories can establish clear goals and targets, paving the way for the implementation of a national HCC surveillance program. While HCC may not have specific WHO goals like hepatitis, countries can draw valuable lessons from the approach taken for other cancer types and tailor them to implement this effectively.

A national HCC surveillance program requires strong support through public education initiatives aimed at driving uptake. A comprehensive network of healthcare professionals, including primary care physicians, public health nurses, and medical workers, is vital for a national HCC surveillance program. Japan's Ministry of Health, Labour and Welfare has taken an impressive approach by training hepatitis medical care coordinators (HMCCs), consisting of various medical professionals, patients, and ordinary citizens. HMCCs act as public advocates, encouraging hepatitis screening, facilitating follow-up care, and raising awareness in workplaces and communities[155]. The JSH also stands out for delivering annual public awareness initiatives such as television programs, workshops for patients and general practitioners, and educational meetings with healthcare professionals. These programs have increased knowledge and awareness of several topics, such as identifying high-risk patients and emphasizing the importance of surveillance for high-risk patients among non-hepatologists and the general public in Japan[105]. Territories can learn from and adapt these programs to local contexts in support of local HCC surveillance efforts.

Efforts to improve treatment access and quality for hepatocellular carcinoma (HCC) patients, particularly those with incurable advanced-stage unresectable HCC who constitute the majority of the HCC patient pool worldwide[156], are crucial alongside HCC surveillance. Excitingly, recent advancements in immune checkpoint inhibitors have shown effectiveness in these patients, representing a paradigm shift in advanced HCC treatment. The combination therapies of atezolizumab-bevacizumab and tremelimumab-durvalumab have been approved by the US Food and Drug Administration, European Medicines Agency and Japan Pharmaceuticals and Medical Devices Agency for advanced unresectable HCC patients who have not undergone prior systemic therapy[157–160]. These approvals were based on clinical trials demonstrating improved overall survival and progression-free survival compared to the previous standard of care, sorafenib[161,162]. Notably, atezolizumab-bevacizumab combination therapy maintained its survival benefits over sorafenib even after additional follow-up[163].

Additionally, the IMbrave150 trial also revealed that atezolizumab-bevacizumab combination therapy also improved quality of life and physical functioning in these patients[164]. Real-world evidence from Thailand, Austria, and Germany also supported the efficacy and quality of life improvements of the atezolizumab-bevacizumab combination therapy[165,166]. Recommendations by global academic societies such as American Society of Clinical Oncology (ASCO), European Society for Medical Oncology (ESMO) and Japan's Clinical Practice Guidelines for Hepatocellular Carcinoma now favor atezolizumab-bevacizumab combination therapy over other monotherapies for unresectable HCC patients who have not undergone prior systemic therapy[156,167,168]. Promising results from the MORPHEUS-liver trial suggest that adding tiragolumab, anti-TIGIT antibody, to atezolizumab-bevacizumab combination therapy may further enhance treatment outcomes[169] for these patients. The global phase 3 clinical trials of this triple therapy comparing atezolizumab-bevacizumab combination, IMbrave152 trial, will be initiated in 2023.

Ongoing and recently concluded clinical trials also explore the potential of immunotherapies in various treatment lines, such as durvalumab-bevacizumab or pembrolizumab-lenvatinib versus TACE in intermediate stage HCC, adjuvant therapy with atezolizumab in combination with bevacizumab[105,170]. Further positive results from these trials and the "ABC conversion therapy" using atezolizumab-bevacizumab combination therapy followed by curative therapy such as resection, ablation or TACE are expected to contribute to improved HCC treatment outcomes[171]. The phase 3 clinical trial, IMPACT trial, to prove the efficacy of ABC conversion therapy will be initiated in 2023.

While these new developments are exciting and can give new hope to patients, access to such innovative treatments will be a challenge for governments and healthcare payers. Combination therapies come at a significant additional cost per patient, so investment will need to be made in order to recognize the benefits of these new treatments.

Japan's experience also underscores the importance of a coordinated approach to address hepatitis and HCC simultaneously.

Specifically, a comprehensive nationwide HCC surveillance program and high quality HCC treatment techniques (which have been detailed in ***section 5***) need to be supplemented with (1) access to hepatitis screening to identify individuals at high risk of HCC; (2) reimbursed antivirals for HCV and HBV (without restrictions); (3) universal HBV vaccination of newborns to significantly reduce the incidence of HCC[24]. Data and technology can be harnessed to optimize these steps and ensure the seamless linkage of patients to care. One way is by implementing an integrated electronic medical record (EMR) system to enable automated screening reminders to be sent to high-risk patients and providers, ensuring timely follow-up and tracking of results, eventually improving patient outcomes.

BOX 6: JAPAN CASE STUDY
The trailblazer and gold standard in managing HCC[35–37,71,105,172,173]

An **accessible nationwide screening program** established in all public hospitals, cancer centers and private practice. This includes the use of ultrasonography and tumour marker screening for high-risk patients (e.g., those with cirrhosis and chronic HBV and HCV). Measurement of all 3 tumour markers (AFP, PIVKA-II, AFP-L3) is covered by insurance and free nationwide testing for HBsAg and HCV Ab is offered at all medical facilities to identify individuals at high risk of HCC.

- Most at-risk patients are screened as healthcare providers will perform periodic screening on patients who test positive for hepatitis every 3-6 months to ensure that HCC is detected at an early stage.

Establishment of **centralized and precise diagnostic and treatment algorithm** among providers has helped to ensure accurate pathological diagnostic criteria for early HCC detection and selection of the best HCC treatment plan respectively.

There is also **increased access and availability to high quality treatment options** including systemic therapy for advanced HCC and high-quality treatment techniques. Japanese healthcare providers have better skill in resection, ablation, TACE and HAIC than other territories and treatment outcomes are the best in the world. A multimodal approach also brings together hepatologists, radiologists, surgeons, and oncologists to design and optimize the best treatment plan. Lastly, interferon treatment, interferon-free DAA treatment for HCV and nucleoside analogue for HBV are specially covered by the Government (100 – 200 USD/month can be paid by patients). Special coverage program of medical expenses, shared by central and local government, has started for patients with HBV or HCV-induced liver cancer and decompensated cirrhosis.

Lastly, a **nationwide registry which consists of comprehensive HCC follow-up data** was implemented by the Liver Cancer Study Group of Japan. This helps to stakeholders to perform effective forward planning to improve the prognosis of HCC. It also clarifies the economic benefits of prevention, screening and treatment.

7.5 ACTION POINT 5: Increase awareness and identify policy champions to drive political commitment

Public awareness-raising activities can effectively create a demand for viral hepatitis and liver cancer services, while also reducing stigma and promoting increased uptake of screening and surveillance[10]. For example, one of the pillars of Japan's successful HCC management involves maintaining high public awareness of HCC and its related risk factors[37]. The Japan Society of Hepatology (JSH) organizes educational lectures multiple times a year to promote public awareness of the importance of early HCC detection through the "Stop the HCC" campaign. Japan has also implemented programs to educate the general public about risk factors associated with HCC, such as HBV and HCV[36].

Furthermore, there is a need to drive awareness and understanding among stakeholders about mother-to-child hepatitis transmission of HBV and prioritize the paediatric population as a vulnerable group for HBV and HCC.

However, as seen as in the example of Taiwan in ***Box 2*** above, HBV screening and treatment programs should not neglect older adults among the general population who did not benefit from HBV birth dose vaccination programs. As HBV remains one of the primary causes of HCC in APAC, policymakers need to be aware that HBV vaccination, whilst being a cost-effective preventive measure, is not a silver bullet to eliminate HBV – it needs to be supported by HBV screening and treatment (integrated within antenatal care programs and HCC surveillance programs). Diabetes is also an important risk factor for HCC development in patients with chronic HBV, and clinicians and researchers can evaluate the feasibility of incorporating diabetes into existing HCC risk stratification systems for chronic HBV patients[174].

Hepatitis (especially HCV) also disproportionately affects marginalized communities, and addressing this issue is often complex and politically sensitive. However, stakeholders across regions should strive for better health equity[10], to align with WHO's 'Strengthening diagnostics capacity' in 'recognizing the need to ensure the integrated and coordinated provision of high-quality, affordable, accessible, age and gender sensitive and evidence-based diagnostic interventions, for all individuals without discrimination, with a view to achieving universal health coverage'[175]. One option is to take a step-wise approach to tackle the hepatitis problem within marginalized communities by initially investing in interventions that target subpopulations within the community that may be more politically acceptable to support (such as ex-offenders in halfway houses or STI/HIV patients)[10]. Learnings and best practices from anti-discriminatory policies, such as Australia's HBV anti-discrimination policy for migrants, can be distilled by stakeholders, including the viral hepatitis community[176].

Strong political will and support from the government have played a crucial role in Japan's best-in-class position in HCC management. Japan has implemented a successful nationwide surveillance system to detect HCC early and has pushed for widespread educational programs to increase awareness of HCC[36,37]. Similarly, strong political commitment in Taiwan has led to a series of discussions and swift response plans for HBV and HCV as detailed earlier in ***Boxes 1*** and ***2.***

A policy champion can also play a crucial role in galvanizing political support for a national hepatitis and HCC program.

This champion does not necessarily have to be a government official or someone holding a senior position but is ideally an individual with a neutral position, whose priorities remain consistent regardless of political changes. For example, in Vietnam, Dr. Phan Huong, the Head of the HIV program, and her team were key advocates and policy champions in securing funding from The Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM), and launching HCV services for PLHIV, PWID, and incarcerated persons in 32 provinces[177].

Regional and local stakeholders can also play a crucial role in galvanizing support by engaging NGOs, patient advocacy groups, and civil society to continuously remind political stakeholders about the importance of health equity. For instance, Yellow Warriors in Philippines were successful in advocating for the implementation of specific clinic days for HBV screening and monitoring at a subnational level.

National initiatives and external funding opportunities can also present policy windows to drive change. For instance, ongoing and upcoming funding rounds from organizations like The Global Fund can trigger discourse about hepatitis and HCC initiatives, generate momentum for action, and provide funding opportunities for national programs[89].

08 Conclusion

This paper has demonstrated the high burden of disease and economic loss associated with liver diseases in APAC. It has also shown the potential upside from tackling these challenges, with estimates ranging from a return on investment of 1.6 - 2.23 per dollar spent, as well as the vast health and societal gains. While the benefits are known and quantified, and the tactics and tools are available, there needs to be a greater urgency to tackle a set of diseases that are still causing the death of ~1.5 million people in APAC every year.

We have laid out a five-point plan to address gaps in the hepatitis and liver cancer landscapes across APAC, starting with developing or enhancing national action plans, and targeting awareness, political will, funding, screening, surveillance, and linkage to care. If these actions can be taken, we can expect to see territories moving closer to the target of elimination of hepatitis and a providing curative treatment for residual HCC patients.

Every stakeholder in the ecosystem, from Ministries of Health, policymakers and funders, industry and providers, or physicians, caregivers and patients, has something to offer, and something to gain.

It will be critical for all of these stakeholders to work together to tackle the problems faced, especially in lower-income territories where resources are sparse.

The APAC Liver Alliance is a multi-lateral group which aims to unite all stakeholders on the mission to counter the rising liver diseases epidemic in the APAC region.

To find out more about their work or to get involved, please contact:

info@apacliverdiseasealliance.org

Investing in these diseases offers not only a chance to reduce pain, suffering and death for millions every year, but also a positive return on investment. It's long past time for all of us to work together to make this happen.

09 Appendix

SCORECARD METHODOLOGY

A targeted literature review of international and national sources in journal publications, symposiums such as the Hepatitis C Virus Elimination Symposium and Solidarity for Hepatitis Elimination, and authoritative websites such as the Coalition for Global Hepatitis Elimination territory dashboard and Polaris Observatory was conducted to identify key frameworks that were previously used to evaluate policy and programs for hepatitis elimination and HCC control. Search results were limited to medical journal articles, authoritative websites and symposiums published or taking place in the past five years.

We analyzed the most relevant sources identified through the targeted literature review and derived a draft set of indicators with which to benchmark hepatitis elimination and HCC control policy and programs in the 13 APAC territories. The goal was to identify policy and program building blocks that are associated with hepatitis elimination progress, high-quality care and good patient outcomes. These form the basis of the indicators, which are clustered into domains.

Subsequently, we created scoring schema based on the indicators, then conducted secondary research using a range of international and national sources to assess and score each of the 13 APAC territories. Scoring judgements were made based on the best information available. Scores for each indicator were summed up and presented as a proportion of the total possible score in the scorecard results. Leading hepatitis and HCC experts then reviewed and advised on the indicators and scorecard through a roundtable discussion, one-on-one discussions and email correspondence. This culminated in a set of 6 HCC indicators and 7 hepatitis indicators to evaluate each territory across 4 domains – (1) national action plan (hepatitis) / national surveillance program (HCC), (2) funding, (3) political commitment, (4) national plan (hepatitis) / surveillance program (HCC) implementation.

HEPATITIS B SCORECARD

Domain	Hepatitis Assessment Indicators	Scoring criteria	Source
National action plans	Presence of National Action plans for hepatitis B	1 = Updated National plan exists for HBV 0.5 = National plan is out of date / embedded within broader plan for STI/HIV 0 = No National plan	Coalition for Global Hepatitis Elimination (CGHE) Country Dashboards and individual country documents or publications
	Clear goals and targets to reduce the burden of hepatitis B	1 = HBV elimination goal	
		1 = HBV treatment target	
		1 = HBV diagnosis targets	
Funding and access	Clear budget allocation for the National Action Plan, for prevention, screening, diagnosis and treatment of HBV	1 = Financial plan included in national action plan	CGHE Country Dashboards and individual country documents or publications
	Presence of sustainable long-term government/ domestic funding for prevention, screening, diagnosis and treatment correlating to affordability/ access	**Presence of funded HBV vaccination services** 1 = Free HBV vaccines provided nationwide 0 = Vaccines are not provided free	
		Presence of reimbursed/ publicly funded screening for HBV 3 = National reimbursed screening 2 = Organized provincial screening program(reimbursed) 1 = Opportunistic reimbursed screening 0 = No reimbursed screening	Individual country documents or publications
		Presence of reimbursed/ publicly funded testing/diagnostic services for HBV 2 = Free testing provided in most settings nationwide with minimal restrictions 1 = Subsidized testing provided/ free testing provided at selected regions 0 = Predominantly out-of-pocket nationwide, with free testing only provided as part of programmatic/ community-based pilots (i.e. for selected sites/ sub-populations)	
		Treatment coverage of HBV treatment 1 = Predominantly government-financed, either on a national level as part of UHC or selected states 0 = Predominantly out-of-pocket	
Political Commitment	Level of political commitment to curb/ manage the growing burden of hepatitis and aiming towards elimination	**HBV elimination progress** 1 = Expect to eliminate HBV by 2030 0 = Expect to eliminate HBV by 2031-2050	CDC Polaris
		Institutional commitment for HBV 2 = Presence of a hepatitis taskforce/ministry/agency or plan that coordinates national multisectoral hepatitis elimination efforts 1 = Presence of a hepatitis taskforce/ministry/agency or plan that only coordinates provincial multisectoral hepatitis elimination efforts 0= No coordination at national or provincial level elimination efforts are decentralized and organized by individual organizations	Individual country documents or publications
		Implementation of policies for HBV or government support for partnerships/initiatives for HBV in past 2 years 2 = Government has implemented national policies or supported partnerships/initiatives in past 2 years 1 = Government has implemented provincial policies or supported partnerships/initiatives in past 2 years 0 = No publicly available information	
Implementation of elimination efforts	HBV vaccination, diagnostic and treatment rate	**>3 Birth dose national vaccination (HBV) uptake** 2 = ≥90% 1 = <90%	CDC Polaris
		HBV diagnostic uptake rate 3 = >50% 2 = 20% - 50% 1 = <20%	
		HBV treatment uptake rate 3= >10% 2= 5-10% 1= <5%	
	Lack of services and programs tailored to the needs of affected populations in different settings	**Tailored efforts/ initiatives (e.g. prenatal screening, elimination of MTCT) to combat HBV for 'mainstream/ general' high risk populations (e.g. pregnant women, co-morbidities)** 3 = Tailored centralized efforts rolled out at a national level 2 = Tailored decentralized efforts seen at a regional level (i.e. rolled out in few regions) but not centrally coordinated 1 = Smaller-scale pilot efforts seen (e.g. 1 effort countrywide, 1-2 regions) at selected pilot sites for selected sub-group/ community, with the intent to expand nationwide or to other regions	Individual country documents or publications

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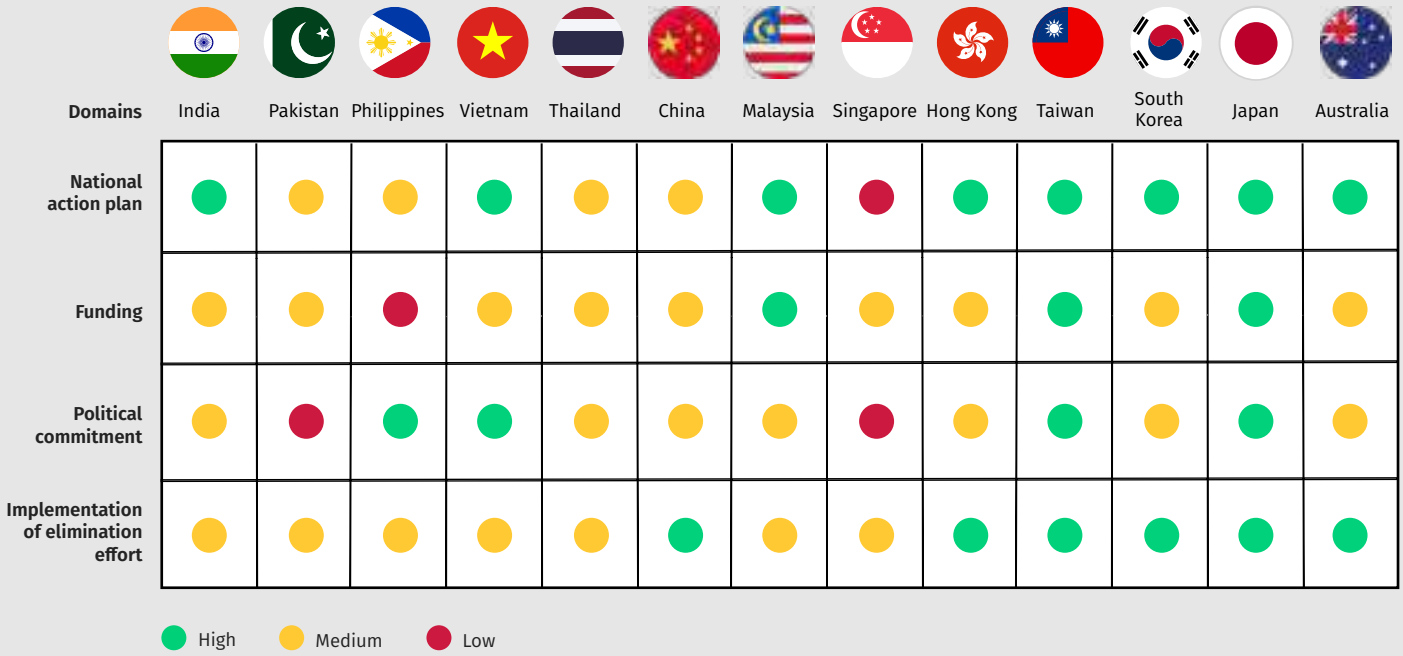
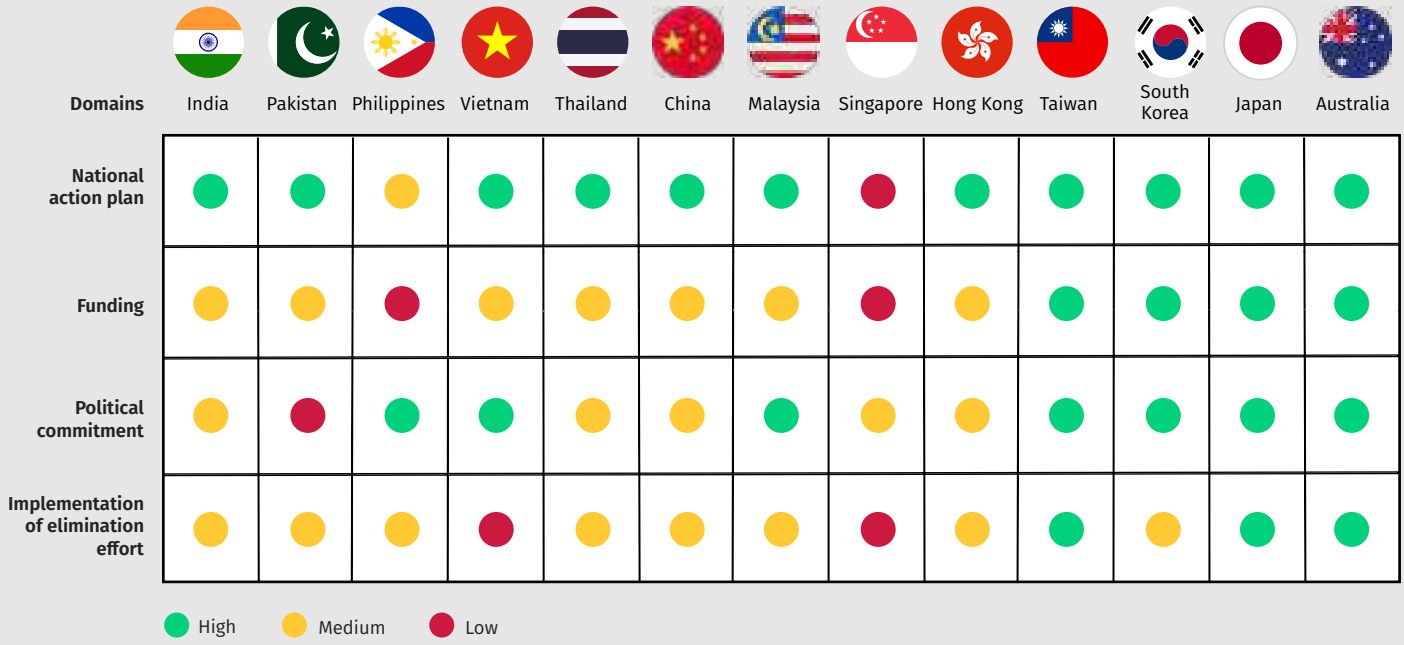
HEPATITIS B SCORECARD RESULTS FOR ALL TERRITORIES



HEPATITIS C SCORECARD

Domain	Hepatitis Assessment Indicators	Scoring criteria	Source
National action plans	Presence of National Action plans for hepatitis C	1 = Updated National plan exists for HCV 0.5 = National plan is out of date / embedded within broader plan for STI/HIV 0 = No National plan	CGHE Country Dashboards and individual country documents or publications
	Clear goals and targets to reduce the burden of hepatitis C	1 = HCV elimination goal	
		1 = HCV treatment target	
		1 = HCV diagnosis targets	
Funding and access	Clear budget allocation for the National Action Plan, for prevention, screening, diagnosis and treatment of HCV	1 = Financial plan included in national action plan	CGHE Country Dashboards and individual country documents or publications
	Presence of sustainable long-term government/ domestic funding for prevention, screening, diagnosis and treatment correlating to affordability/ access	**Presence of reimbursed/ publicly funded screening for HCV** 3 = National reimbursed screening 2 = Organized provincial screening program (reimbursed) 1 = Opportunistic reimbursed screening 0 = No reimbursed screening	Individual country documents or publications
		Presence of reimbursed/ publicly funded testing/diagnostic services for HCV 2 = Free testing provided in most settings nationwide with minimal restrictions 1 = Subsidized testing provided/ free testing provided at selected regions 0 = Predominantly out-of-pocket nationwide, with free testing only provided as part of programmatic/ community-based pilots (i.e. for selected sites/ sub-populations)	
		Treatment coverage of HCV treatment 1 = Predominantly government-financed, either on a national level as part of UHC or selected states 0 = Predominantly out-of-pocket	
Political Commitment	Level of political commitment to curb/ manage the growing burden of hepatitis and aiming towards elimination	**HCV elimination progress** 1 = Expect to eliminate HCV by 2030 0 = Expect to eliminate HCV by 2031-2050	CDC Polaris
		Institutional commitment for HCV 2 = Presence of a hepatitis taskforce/ministry/agency or plan that coordinates national multisectoral hepatitis elimination efforts 1 = Presence of a hepatitis taskforce/ministry/agency or plan that only coordinates provincial multisectoral hepatitis elimination efforts 0= No coordination at national or provincial level elimination efforts are decentralized and organized by individual organizations	Individual country documents or publications
		Implementation of policies for HCV or government support for partnerships/initiatives for HCV in past 2 years 2 = Government has implemented national policies or supported partnerships/initiatives in past 2 years 1 = Government has implemented provincial policies or supported partnerships/initiatives in past 2 years 0 = No publicly available information	
Implementation of elimination efforts	HCV diagnostic and treatment rates	**HCV diagnostic uptake rate** 4 = >80% 3 = 50% - 80% 2 = 20% - 50% 1 = <20%	CDC Polaris
		HCV treatment uptake rate 3= >10% 2= 5-10% 1= <5%	
	Lack of services and programs tailored to the needs of affected populations in different settings	**Efforts/ initiatives to combat HCV among marginalized high risk populations (PLHIV, PWID, MSM, indigenous, incarcerated populations, foreign workers)** 3 = Tailored centralized efforts rolled out at a national level 2 = Tailored decentralized efforts seen at a regional level (i.e. rolled out in few regions) but not centrally coordinated 1 = Smaller-scale pilot efforts seen (e.g. 1 effort countrywide, 1-2 regions) at selected pilot sites for selected sub-group/ community, with the intent to expand nationwide or to other regions	Individual country documents or publications

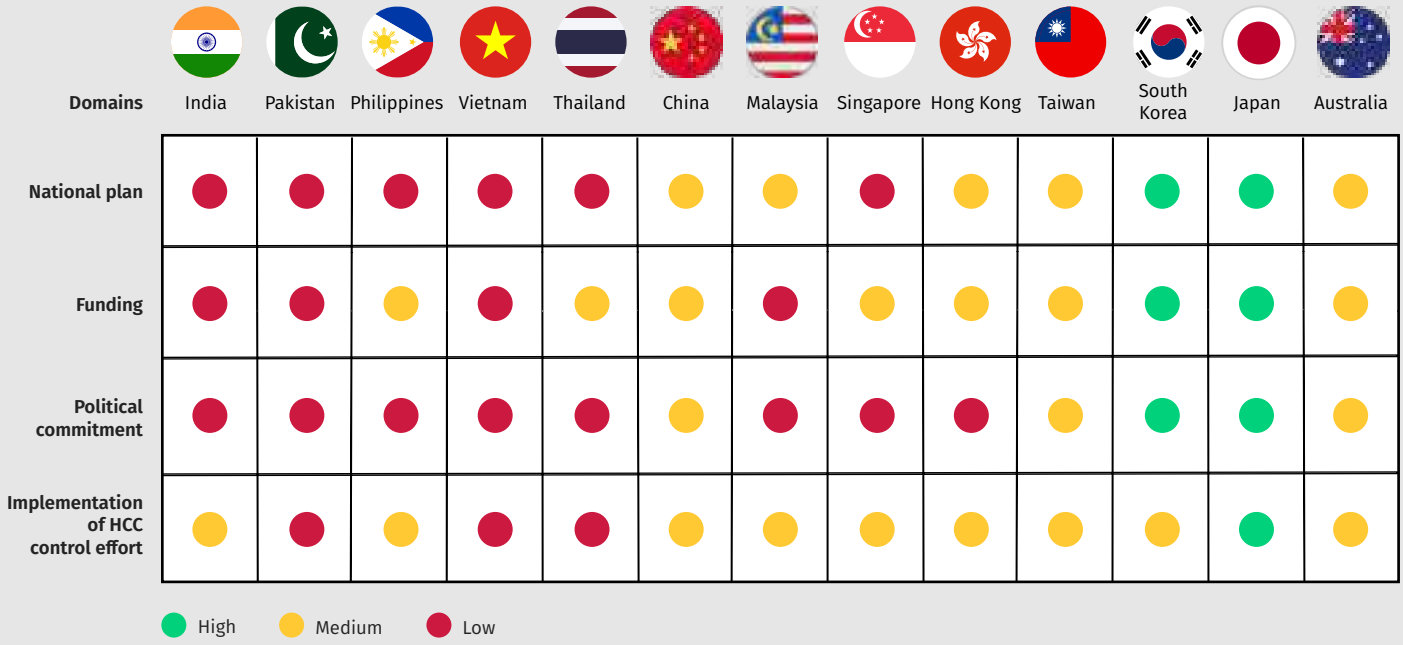
HEPATITIS C SCORECARD RESULTS FOR ALL TERRITORIES



HCC SCORECARD

Domain	HCC Assessment Indicators	Scoring criteria	Source
Comprehensive national plan	Presence of a comprehensive national screening program or strategy for HCC	2 = National population-based HCC screening or surveillance program/ plan exists (e.g. National Liver Cancer Surveillance Program in Korea and regular follow-ups by the Liver Cancer Study Group of Japan) 1 = HCC screening program/ plan is limited to specific regions (i.e. not implemented nationwide)	Individual country documents or publications
	Inclusion of liver cancer in national cancer strategic or control plan	1 = Liver cancer is included/ mentioned in the national cancer control plan	
Funding and access	Presence of a sustainable long-term funding (external or domestic) for surveillance, prevention, diagnosis and treatment of HCC	3 = Government reimbursement for HCC screening, Dx, follow-up (3 biomarkers - AFP, PIVKA-II, AFP-L3) 2 = Government reimbursement for HCC screening, Dx, follow-up (2 biomarkers) 1 = Government reimbursement for HCC screening, Dx, follow-up (1 biomarker only)	Individual country documents or publications
		2 = Immunotherapy approved and reimbursed for HCC 1 = Immunotherapy approved but not reimbursed for HCC 0 = no data found/no immunotherapy approved for HCC	
Political Commitment	Level of political commitment to stop the growing burden of HCC	**Expressed commitment** 1 = Expression of verbal declarations/ statements of support for liver cancer/HCC by an influential political leader OR expressed support for or approved reimbursement of at least 1 high cost immunotherapy for liver cancer	Individual country documents or publications
		Institutional commitment 3 = Recent institutional commitment (national or government): Earmarked allocation of resources towards HCC or organizational infrastructure/ task force put in place 2 = Recent institutional commitment (limited to certain country regions/provinces or non-governmental): Earmarked allocation of resources towards HCC or organizational infrastructure/ task force put in place 1 = Past institutional commitment (>10 yrs ago) without recent updates	
Implementation of HCC control efforts	Presence of comprehensive strategies for HCC diagnosis/ screening, monitoring and surveillance	**High risk groups who should be recommended HCC surveillance based on local guidelines or practice:** 2 = Cirrhotic patients and those with chronic HBV or HCV 1 = Cirrhotic patients and those with chronic HBV 0 = No consensus	Individual country documents or publications
		HCC screening/diagnosis 4 = Sonography with 3 biomarkers tracked 3 = Sonography with 2 biomarkers tracked 2 = Sonography with 1 biomarker tracked 1 = Sonography without biomarker tracking	
		HCC monitoring 4 = Ultrasound + 3 biomarkers every 3-4 months for high-risk patients or every 6 months for extremely high-risk patients 3 = Ultrasound + 2 biomarkers every 3-4 months for high-risk patients or every 6 months for extremely high-risk patients 2 = Ultrasound + 1 biomarkers every 3-4 months for high-risk patients or every 6 months for extremely high-risk patients 1 = Ultrasound every 6-12 months for high-risk patients 0 = Unknown	
	Update frequency and level of comprehensiveness of clinical guidelines for HCC management including surveillance	**Clinical guidelines update** 2 = Up to date comprehensive national clinical guidelines with frequent/ recent updates in HCC management 1 = Less comprehensive clinical guidelines launched by smaller individual research groups/ non-liver cancer specific groups, with some probable variations between guidelines vs practice	

HCC SCORECARD RESULTS FOR ALL TERRITORIES



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APAC Hepatocellular Carcinoma Policy Forum 2024

Bangkok October 2, 2024

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

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2024 Hepatocellular Carcinoma APAC Policy Forum

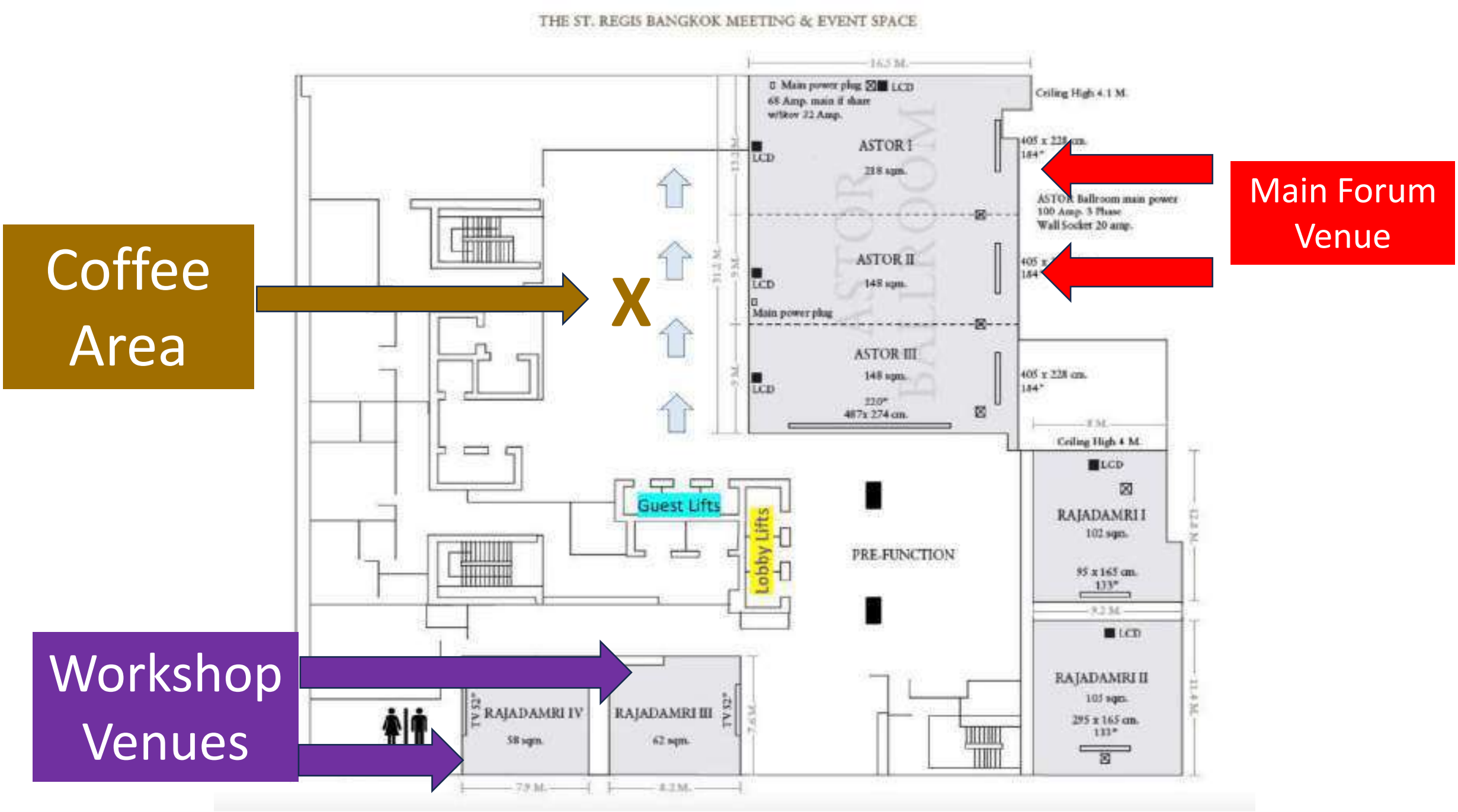
October 2, 2024 | Bangkok, Thailand

Agenda

Time	Agenda Item	Title	Speaker
9.00- 9.10 am	Welcome	**Setting the Stage:** Addressing HCC in APAC – A Multistakeholder and Multilateral Approach	**Ms. Roberta Sarno** Director, APAC Liver Disease Alliance
9.10- 9.20 am	Keynote 1	**Prioritising HCC in Public Health:** Insights from Thailand's Ministry of Public Health	**Dr. Sakarn Bunnag** Deputy Director General, Department of Medical Services, Ministry of Public Health, Thailand
9.20- 9.30 am	Opening Address	**Remarks by Dr. Christine Ross**	**Director, CDC Thailand Director** US Embassy Bangkok
9.30- 9.40 am	Keynote 2	**Strategies for HCC Elimination in Japan:** A Policy Perspective from the Japan Society of Hepatology	**Prof. Tatsuya Kanto** Director, Research Center for Hepatitis and Immunology, National Center for Global Health and Medicine, Japan Japan Society of Hepatology
9.40- 9.50 am	Lecture 1	**Epidemiology, Clinical and Economic Burden of HCC in APAC:** Urgent Call for Enhanced Recognition, National Plans and Patient Journey Insights	**Mr. Will Brown** Senior Director, Vista Health
9.50- 10.10 am	Lecture 2	**A Clinician's Perspective:** Management of HCC in Japan as a Leading Model	**Prof. Masatoshi Kudo** Professor & Chairman, Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine Japan Society of Hepatology

Time	Agenda Item	Title	Speaker
10.10 - 10.20 am **Coffee & Networking**			
10.20-10.30 am	Lecture 3	**A Health Ministry's Perspective:** Measures Against Liver Disease in Japan	**Dr. Soichiro Kiyono** Assistant Director, Hepatitis Prevention and Control Office, Ministry of Health, Labour and Welfare, Japan
10.30-10.40 am	Lecture 4	**Optimising HCC Surveillance:** Clinical and Economic Benefits of PIVKA-II, Digital Algorithms and Enhanced Patient Therapy and Care	**Prof. Pisit Tangkijvanich** Head, Center of Excellence in Hepatitis & Liver Cancer, Chulalongkorn University
10.40 - 11.00 am **Coffee & Networking**			
11.00 am-12.00 pm	Panel 1	**Progress Report:** HCC Surveillance and Management Across APAC	**Moderator: Prof. Masatoshi Kudo** 1. **Dr. Murallitharan Munisamy –** Managing Director, National Cancer Society Malaysia (Malaysia). 2. **Ms. Do Thi Ngat** – Officer, Health Protection Division, Medical Service Administration Department, Ministry of Health (Vietnam). 3. **Prof. Dr. Teerha Piratvisuth** – Chairman, Scientific Program, Thai Association for the Study of the Liver (Thailand). 4. **Prof. Simone Strasser** – Head of Department & Senior Staff Specialist, AW Morrow Gastroenterology and Liver Centre, Royal Prince Alfred Hospital (Australia). 5. **Dr. Somchai Thanasitthichai, M.D.** – Director, Thailand National Cancer Institute, Ministry of Public Health (Thailand). 6. **Dr. Shi-Lun Wei –** Deputy Director-General Health Promotion Administration, Ministry of Health and Welfare (Taiwan). 7. **Ms. Wen-Wen Yang** – Advisor and Lecturer, Taiwan Alliance of Patients' Organization (Taiwan).
12.00 - 1.00 pm **Networking Lunch**			

Time	Agenda Item	Title	Speaker
1.00 - 1.20 pm **Photo Session**			
1.20- 2.20 pm	Panel 2	**Success Stories:** Effective Practices in HCC Surveillance and Management	**Moderator: Ms. Roberta Sarno** 1. **Prof. Chien-Jen Chen** – Academician & Distinguished Professor, Genomics Research Center, Academia Sinica (Taiwan). 2. **Prof. Jacob George** – Head, Gastroenterology & Hepatology Department, Westmead Hospital (Australia). 3. **Prof. Tatsuya Kanto** – Director, Research Center for Hepatitis & Immunology, National Center for Global Health and Medicine; Japan Society of Hepatology (Japan). 4. **Prof. Dorothy Keefe** – CEO, Cancer Australia (Australia). 5. **Dr. Norlen Bin Mohamed** – Sector Head, Non-Communicable Disease Sector, Disease Control Division, Malaysia Health Ministry (Malaysia). 6. **Dr. Luckxawan Pimsawadi** – Head, Thai Liver Cancer Patient Group (Thailand). 7. **Dr. Jasmine Pwu** – CEO, Data Science Center, Fu Jen Catholic University (Taiwan). 8. **Dr. Poowanai Sarkhampee** – Hepato-Pancreato-Biliary Surgeon, Senior Professional Level, Division of Hepato-Pancreato-Biliary Surgery and Transplantation, Sunpasitthiprasong Hospital (Thailand).
2.20- 4.20 pm	Workshop	**Co-creating A Roadmap** for Robust National HCC Surveillance and Management Programs in APAC	**Mr. Will Brown**, Senior Director, Vista Health will moderate the Workshop Involvement: All delegates
4.20 - 4.40 pm **Coffee & Networking**			
4.40- 4.50 pm	Closing + Next steps	**Wrapping up:** Reflections and Future Directions	**Ms. Roberta Sarno** Director, APAC Liver Disease Alliance


THE ST. REGIS BANGKOK MEETING & EVENT SPACE
Coffee Area
X
Main Forum Venue
Workshop Venues
ASTOR I
218 sqm.
ASTOR II
148 sqm.
ASTOR III
148 sqm.
ASTOR BALLROOM
Ceiling High 4.1 M.
Ceiling High 4 M.
Guest Lifts
Lobby Lifts
PRE-FUNCTION
RAJADAMRI I
102 sqm.
RAJADAMRI II
103 sqm.
RAJADAMRI III
62 sqm.
RAJADAMRI IV
58 sqm.
LCD
TV 52"

Opening Remarks

Roberta Sarno
APAC Liver Disease Alliance

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

Hepatocellular carcinoma (HCC) is the main type of liver cancer, the fifth most common cancer and the second deadliest in APAC.

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

In 2020, the APAC region reported 610,000 new liver cancer cases, representing 73% of the global incidence.

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

72% of global HCC deaths were attributed to APAC, with a staggering 566,000 reported cases.

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

80% of HCC cases are diagnosed at an advanced stage, negatively impacting treatment outcomes.

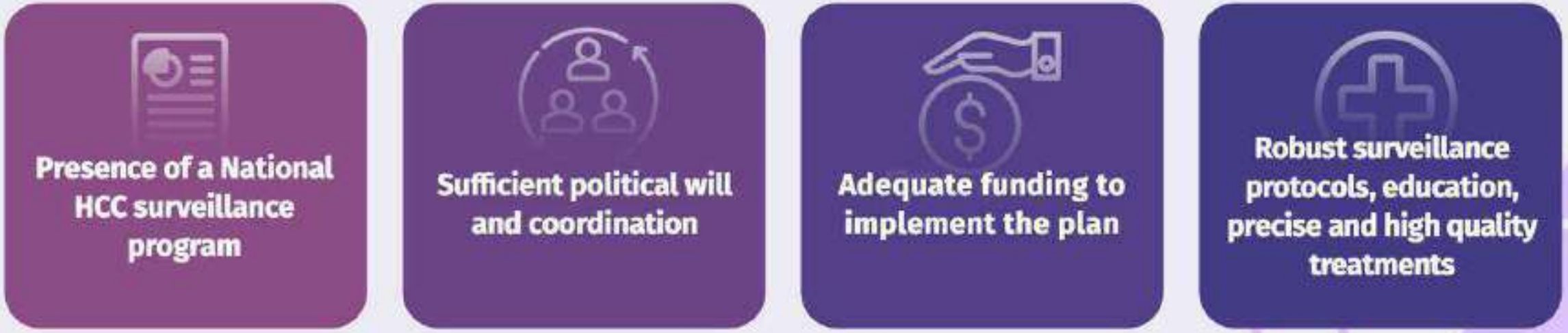
The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

Despite increasing efforts, most APAC territories can do more to better manage HCC.

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

Japan stands out in performance and is perceived as an exemplar in HCC surveillance and management, through which

4 factors have been identified to be the key to HCC management



Source: https://www.apacliverdiseasealliance.org/s/Hepatitis-and-HCC-Elimination-in-APAC_White-Paper.pdf

The power of a multistakeholder and multilateral approach

"Every stakeholder in the ecosystem, from Ministries of Health, policymakers and funders, industry and providers, or physicians, caregivers and patients, has something to offer, and something to gain."

VALUE OF STRONG HEPATITIS ELIMINATION AND HCC SURVEILLANCE PROGRAMS

Patients and their caregivers:

- De-stigmatization
- Improved access to screening, surveillance and treatment
- Chance of curing HCV
- Better prognosis for HBV and HCC

Healthcare professionals:

- Timely and appropriate clinical response
- Confidence in screening and diagnostic results

Governments and the economy:

- Healthier population a better economic productivity
- Reduce absenteeism due to debilitating symptoms associated with chronic HBV and late-stage HCC

Healthcare systems and payors:

- Progress towards UHC
- Increase cost-effectiveness by detecting and treating early
- Enhance economic efficiencies by adding hepatitis screening (and HCC surveillance) to existing health services such as TB, HIV
- Generate cost-effectiveness data using micro-elimination

Healthcare providers:

- Reduce operational costs and set-up time by combining hepatitis screening with other health services for TB/HIV
- Alleviate bed crunch by detecting and treating patients early before progression to chronic HBV and HCC

Source: https://www.apacliverdiseasealliance.org/s/Hepatitis-and-HCC-Elimination-in-APAC_White-Paper.pdf

The time to act is now!

APAC Liver Disease Alliance

A multilateral, multistakeholder neutral platform working to raise awareness, facilitate policy discussions and generate knowledge.

MISSION

“Reduce the growing burden of liver disease and its social and economic impact in APAC.”

OUR MEMBERS

Strategic partners

Coalition for Global Hepatitis Elimination

The Hepatitis Fund

ILCM

Global Liver Institute

Harvard Medical School – Blavatnik Institute Global Health & Social Medicine – Program in Global Primary Care and Social Change

KOLs

Sponsors

Abbott

Roche

AstraZeneca

Knowledge partners

vista health

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

Thank you!

info@apacliverdiseasealliance.org

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

APAC Hepatocellular Carcinoma Policy Forum 2024

Bangkok October 2, 2024

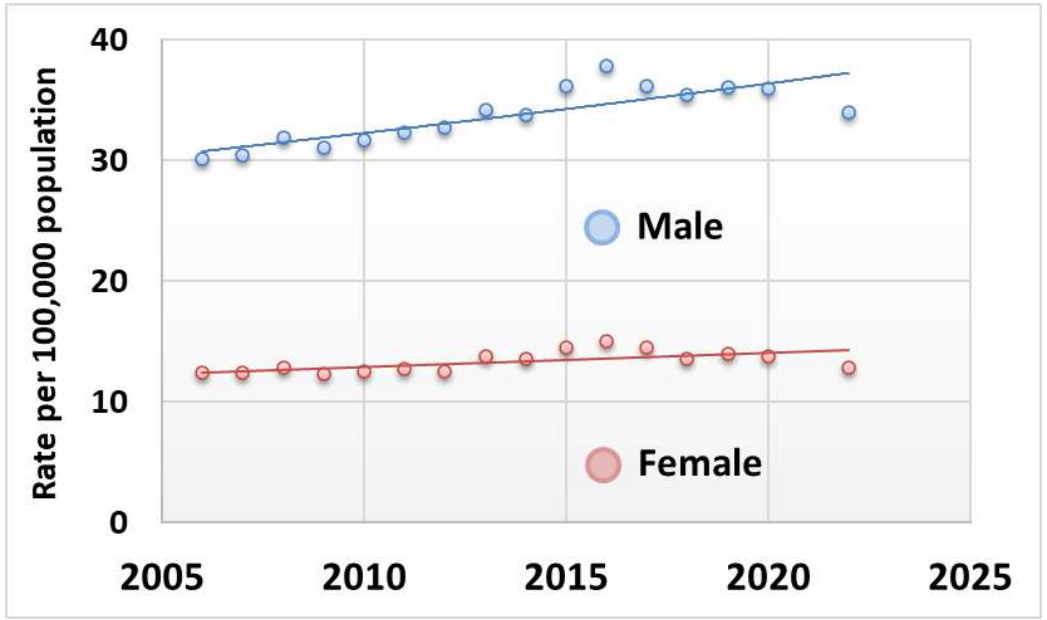
The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

Prioritizing HCC in public health: Insights from Thailand's Ministry of Public Health

Dr. Sakarn Bunnag
Deputy Director, Department of Medical Services, Ministry of Public Health

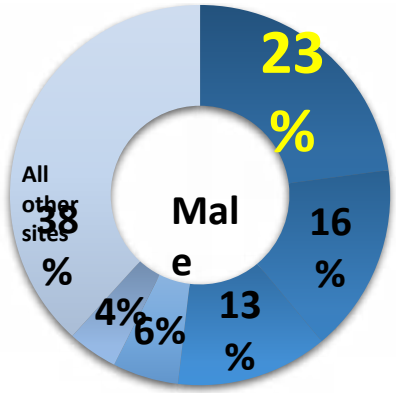
Hepatocellular Carcinoma (HCC) in Thailand

Mortality trends of liver cancer in Thailand (1)

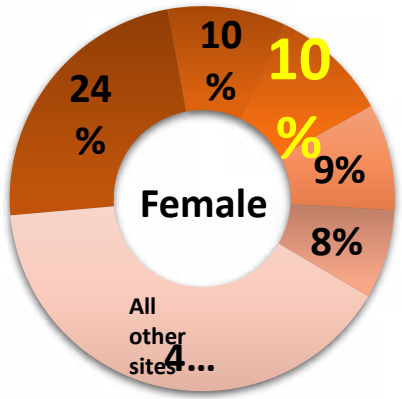


- Leading cause of cancer-related death in Thailand
- Most common cancer in men and the third most common in Thai women
- Approximately 20,000 new cases and 16,000 deaths
- Disease is often diagnosed at advanced stages, limiting treatment options

Top 5 most frequent incident cancers (2)



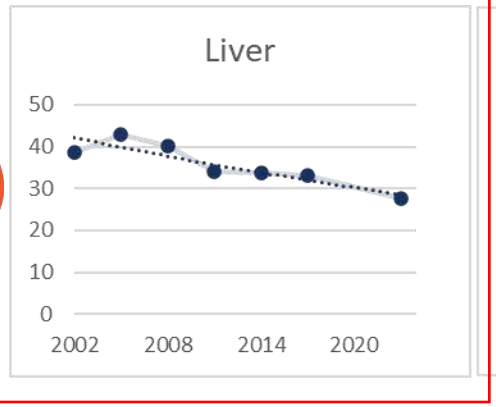
- **Liver and bile duct (23%)**
- Trachea, Bronchus, and lung (16%)
- Colon and rectum (13%)
- Prostate (6%)
- Non-Hodgkin lymphoma (4%)
- All other sites (38%)

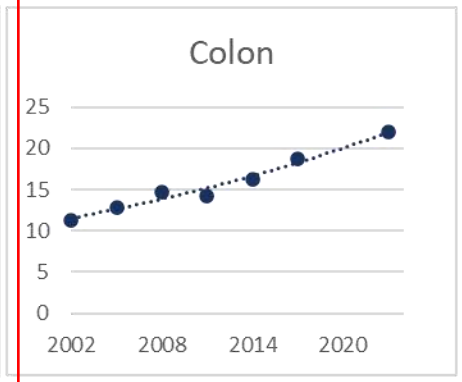


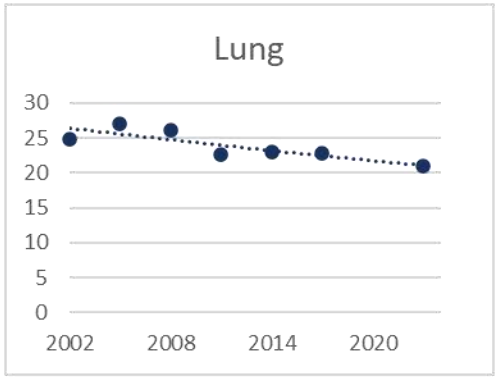
- Breast (24%)
- Colon and rectum (10%)
- **Liver and bile duct (10%)**
- Trachea, Bronchus, and lung (9%)
- Cervix uteri (8%)
- All other sites (40%)

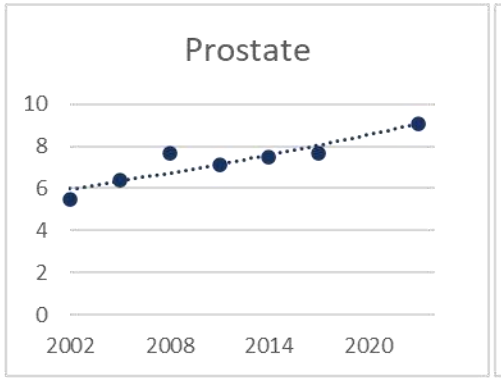
Sources:
(1) Strategy and Planning Division, Office of the Permanent Secretary Ministry of Public Health
(2) Cancer in Thailand (2016-2018), National Cancer Institute

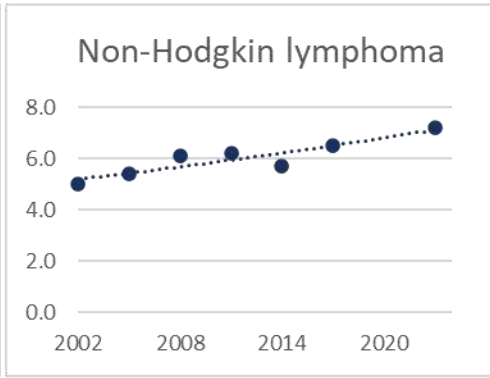
Top 5 cancer incidence trends in Thailand (2002-2023)

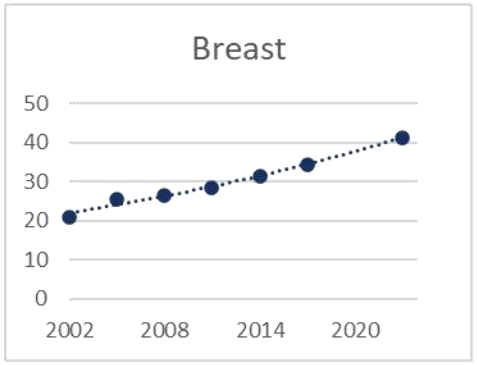


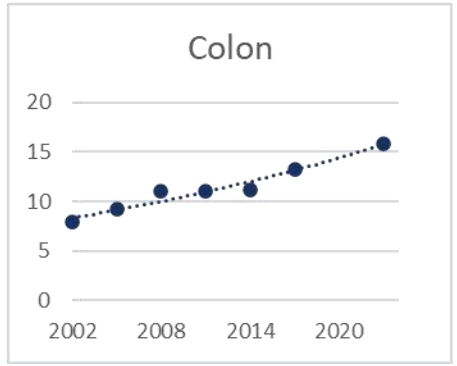


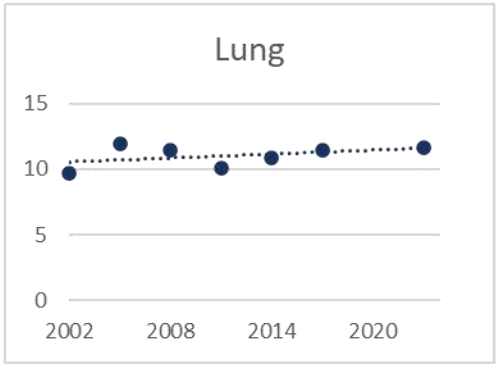


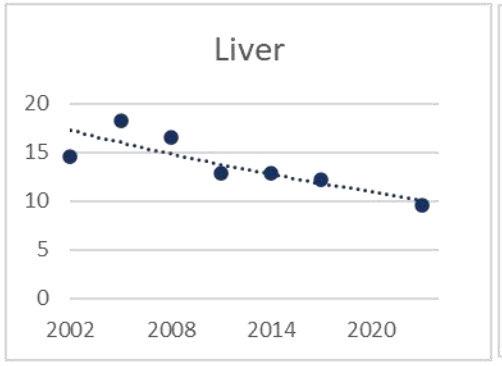


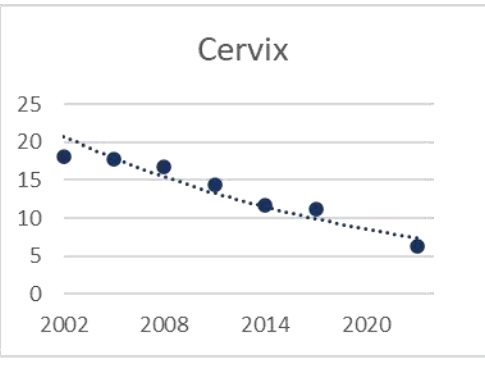






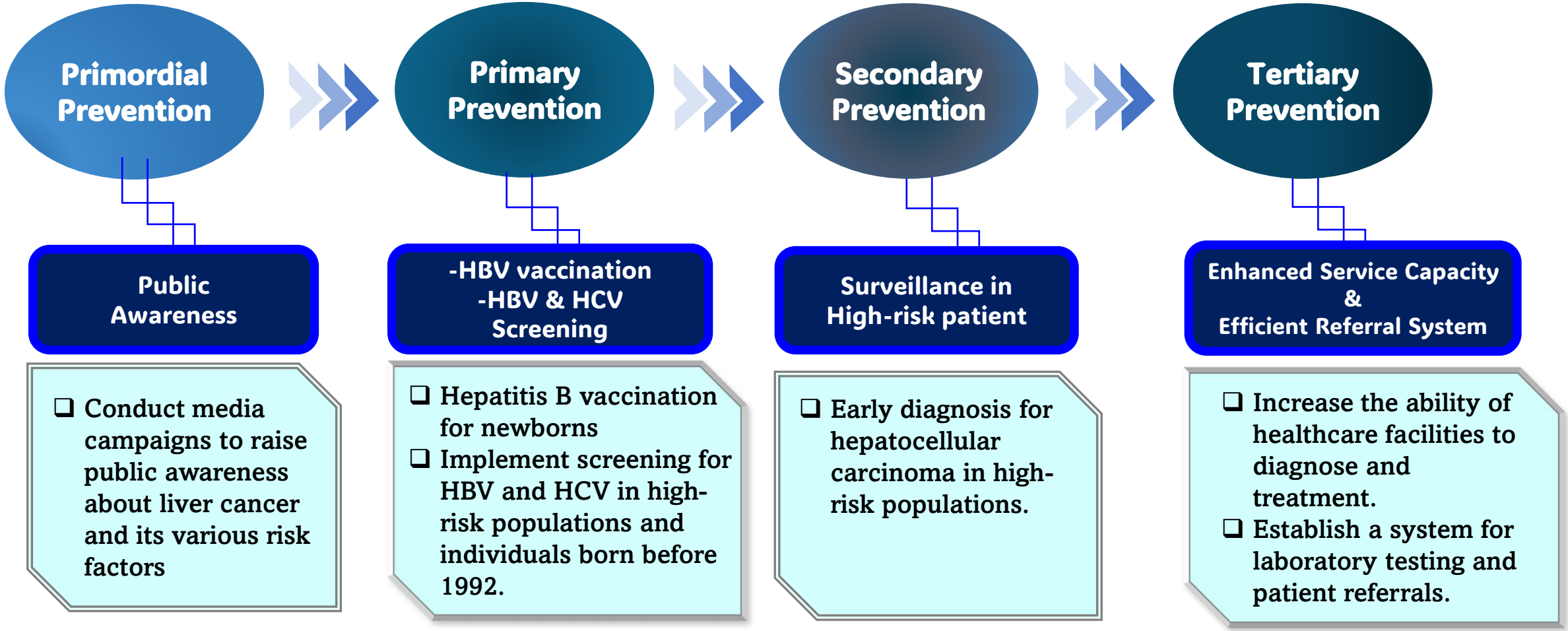






Source: Cancer in Thailand 2002-2018
The 2023 data is a projection

Strategies to Reduce Liver Cancer Burden

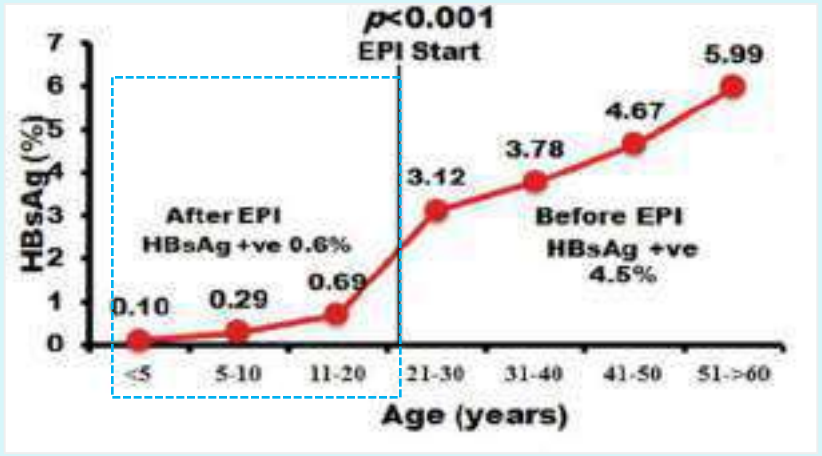


Primary Prevention: HBV vaccination

Most common risk factors of HCC

Chronic HBV infection accounted 49.8% of the total HCC patients
followed by alcohol consumption, chronic HCV infection and cryptogenic cirrhosis [1]

- Hepatitis B vaccination for newborns was introduced in 1992 as part of Thailand's Expanded Program on Immunization (EPI)
- The coverage rate increased from 15% in 1992 to 95% in 2000 and has reached levels of 99% since 2013 [2]
- Hepatitis B prevalence among those born after 1992 is now about 0.6%, significantly reduced due to newborn vaccination [3]



Prevalence of HBV infection by age group [4]

Sources:
(1) Chonprasertsuk (2017), Epidemiology and treatment of hepatocellular carcinoma in Thailand
(2) Leroi et al (2016) Prevalence of chronic hepatitis B virus infection in Thailand: a systematic review and meta-analysis
(3) Thailand National Strategies to Eliminate Viral Hepatitis 2022 – 2030
(4) Posuwan et al (2016), The Success of a Universal Hepatitis B Immunization Program as Part of Thailand's EPI after 22 Years' Implementation

Primary Prevention: HBV, HCV screening

Key Measures:

Screening for HBV and HCV among individuals aged 35-55 to facilitate early treatment and monitoring for liver cancer.

Target in 2024:

1 million people aged 35-55 will be screened and treated for hepatitis B and C.

Quarterly Activities and target

Target population: Thai people aged 35-55 years

Quarter 1

- Communicate policy on hepatitis B and C screening and treatment.
- Establish a screening and referral system in each province.
- Target populations get screened for hepatitis B and C **(100,000, 10% of the target population)**

Quarter 2

- **Develop guidelines for HBV/HCV** treatment to improve access.
- Target populations get screened for hepatitis B and C **(200,000, 20%)**
- **80%** of those diagnosed with hepatitis B and C receive treatment.

Quarter 3

- Target populations get screened for hepatitis B and C **(400,000, 40%)**
- **80%** of those diagnosed with hepatitis B and C receive treatment.
- Organize the screening campaigns for targeting at-risk groups
- Organize activities to raise awareness about prevention and screening

Quarter 4

- Target populations get screened for hepatitis B and C **at least 700,000, 70%**
- Enhance and expand campaigns to achieve the screening of **1 million people.**
- More than 80% of those diagnosed with hepatitis B and C receive treatment.

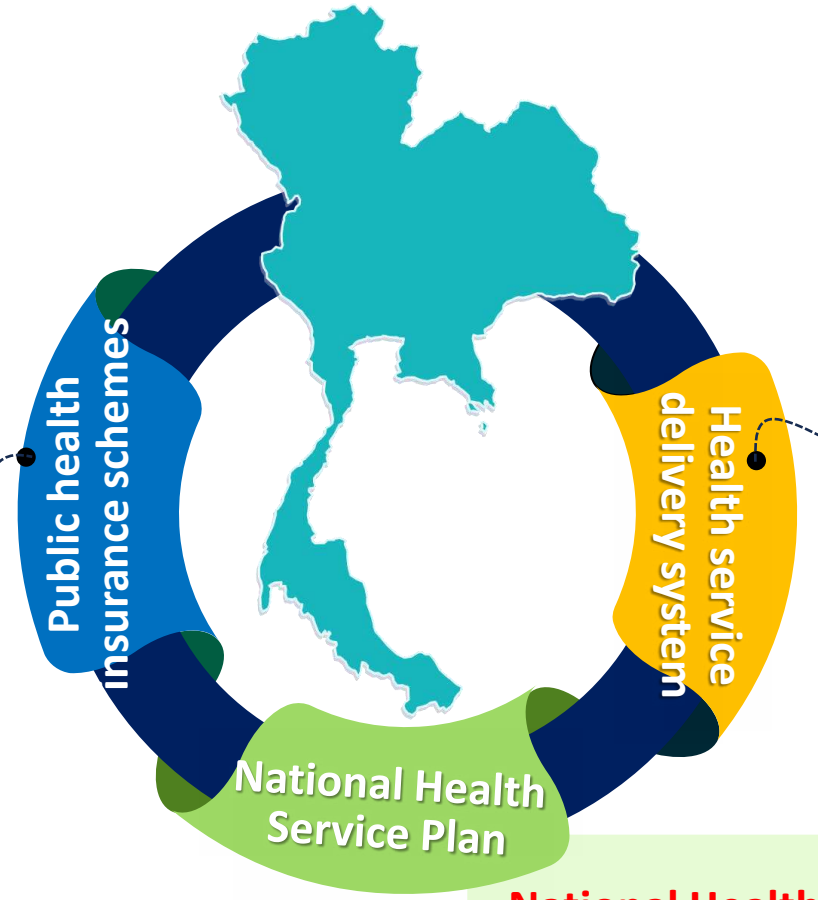
Financial and infrastructure

Three public health insurance schemes

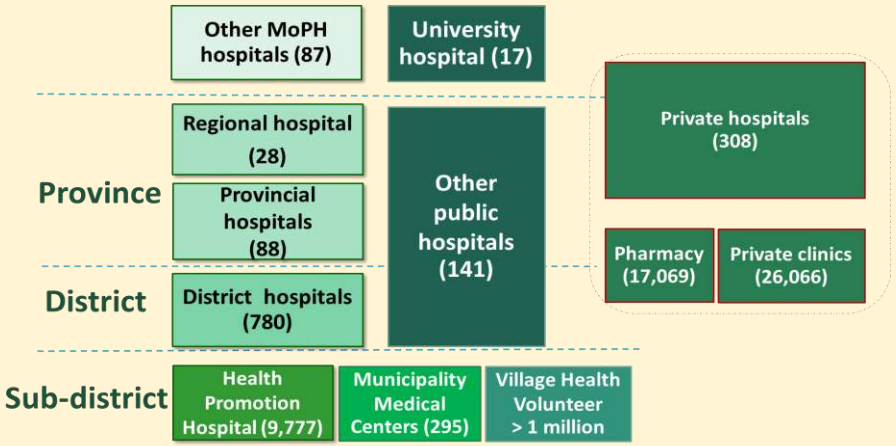
Universal Coverage Scheme (UCS)
51.1 million (75.7 %)

Social Health Insurance (SHI)
11.6 million (17.2 %)

Civil Servant Medical Benefit Scheme (CSMBS)
4.8 million (7.1 %)



Health service delivery system



National Health Service Plan:

Health regions in Thailand were divided into 12 groups of provinces plus Bangkok.

To collaborate efforts among every department and community-based unit from primary to super tertiary care.

3S

- Self-Contain
- Sharing Resources
- Seamless Service

Health Outcome
Reduction of incidence, mortality and waiting times

Thank you
for your attention

APAC Hepatocellular Carcinoma Policy Forum 2024

Bangkok October 2, 2024

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

U.S. government support for combating HCC

Dr. Christine Ross
Country Director/DGHP Program Director for Thailand
Centers for Disease Control and Prevention

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STRATEGIES FOR HCC ELIMINATION IN JAPAN:

A Policy Perspective from the Japan Society of Hepatology

PROF. TATSUYA KANTO

Research Center for Hepatitis and Immunology,

National Center for Global Health and Medicine

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

Financial disclosures

- Speaker/consulting fees:
  - Gilead Sciences,
  - GSK
- Research fund:
  - Aska Pharmaceutical Co., Ltd.

EALA (East Asia Liver Alliance) for combating liver disease in east Asia - JSH-KASL-TASL collaboration

MEMORANDUM OF UNDERSTANDING
BETWEEN
KOREAN ASSOCIATION OF THE STUDY OF THE LIVER,
TAIWAN ASSOCIATION FOR THE STUDY OF THE LIVER
AND
THE JAPAN SOCIETY OF HEPATOLOGY

ARTICLE-1: PURPOSE

The purpose of this MOU is to promote a framework for cooperation among KASL, TASL and JSH to develop and implement joint initiatives in areas of common interest.

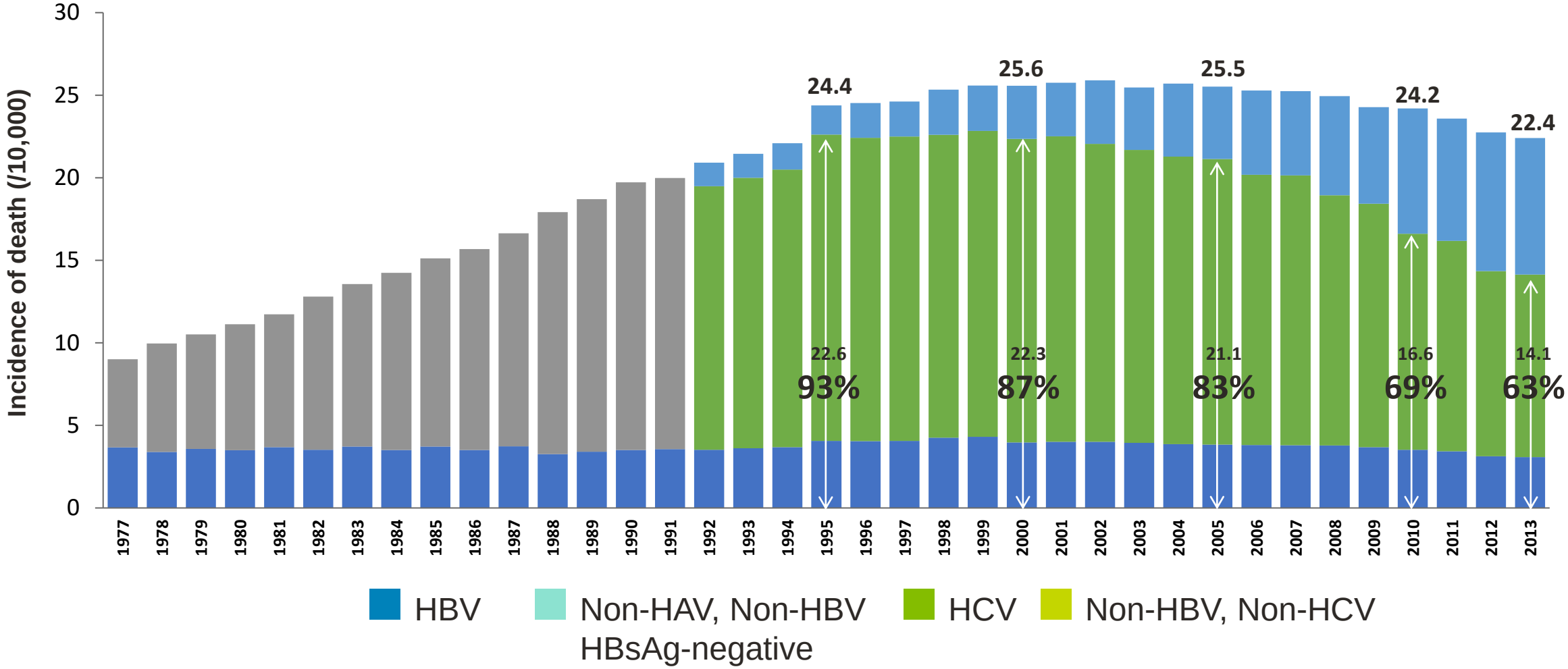
JSH
一般社団法人
日本肝臓学会
The Japan Society of Hepatology

Taiwan Association for the Study of the Liver
TASL

KASL
The Korean Association for the Study of the Liver

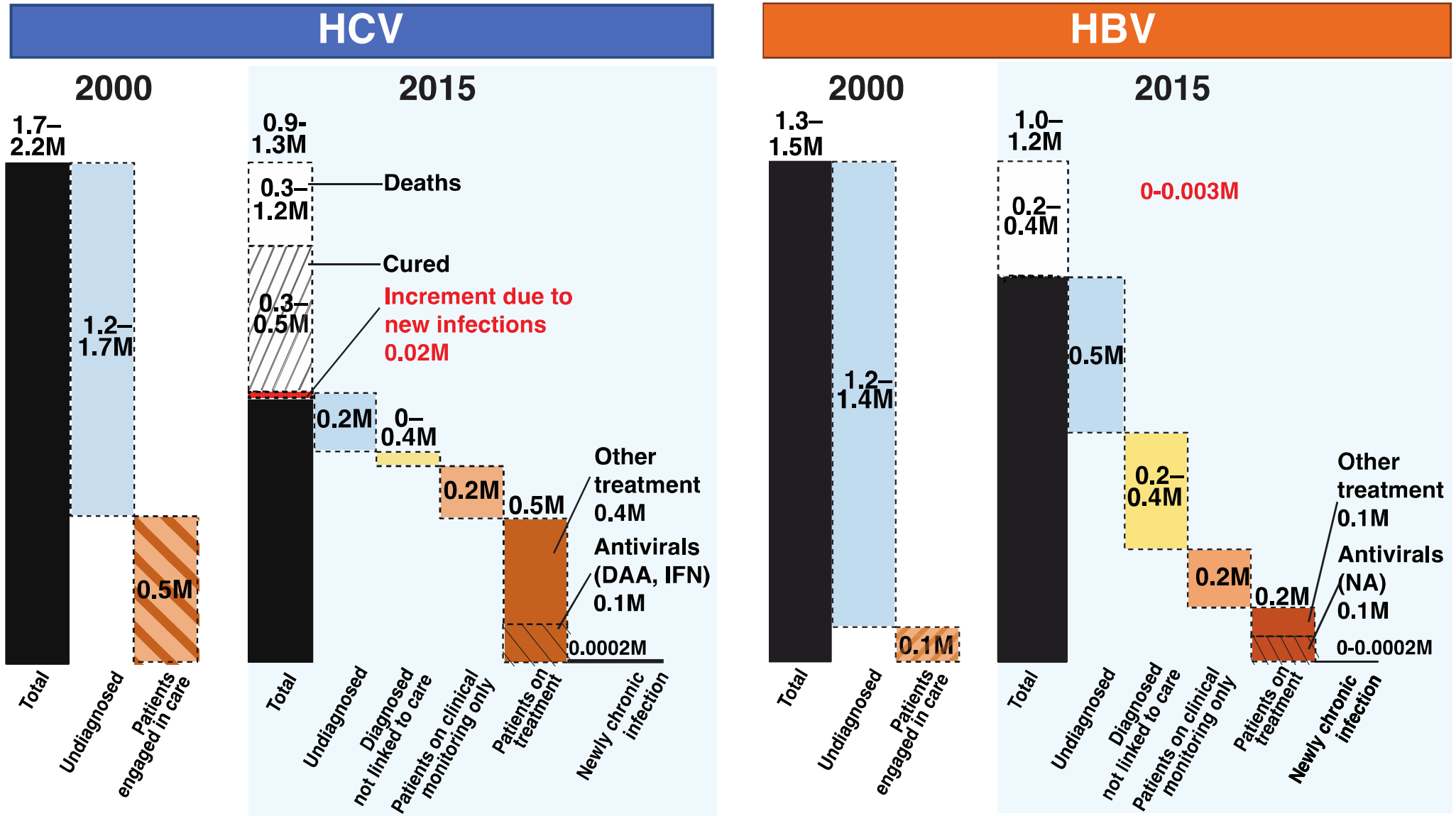
September 22nd, 2023 @Busan

Mortality caused by hepatocellular carcinoma in Japan (1977–2013)

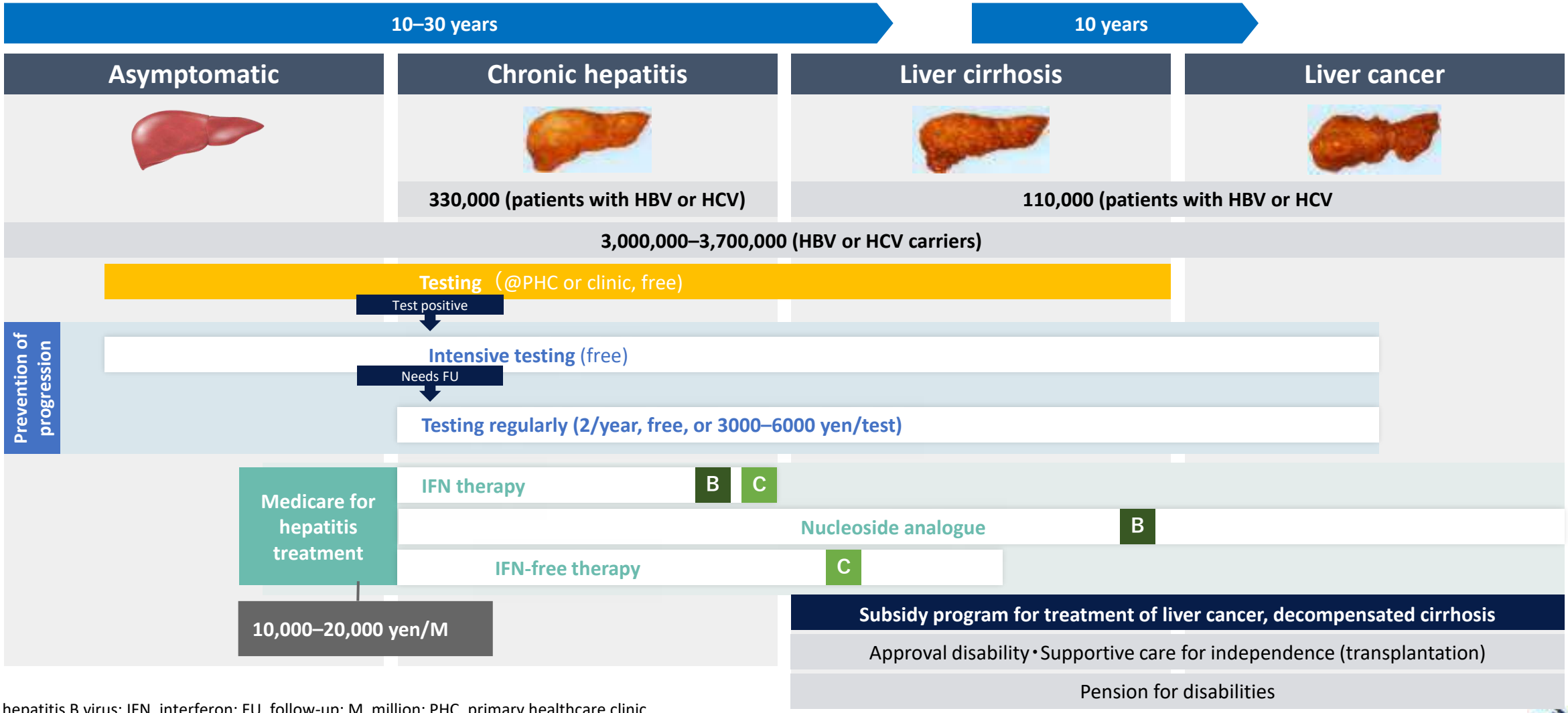


From Census 2013, courtesy of Prof. Junko Tanaka.

Total numbers of HBV or HCV carriers in Japan (2000-2015)



National Hepatitis Programs in Japan 2024



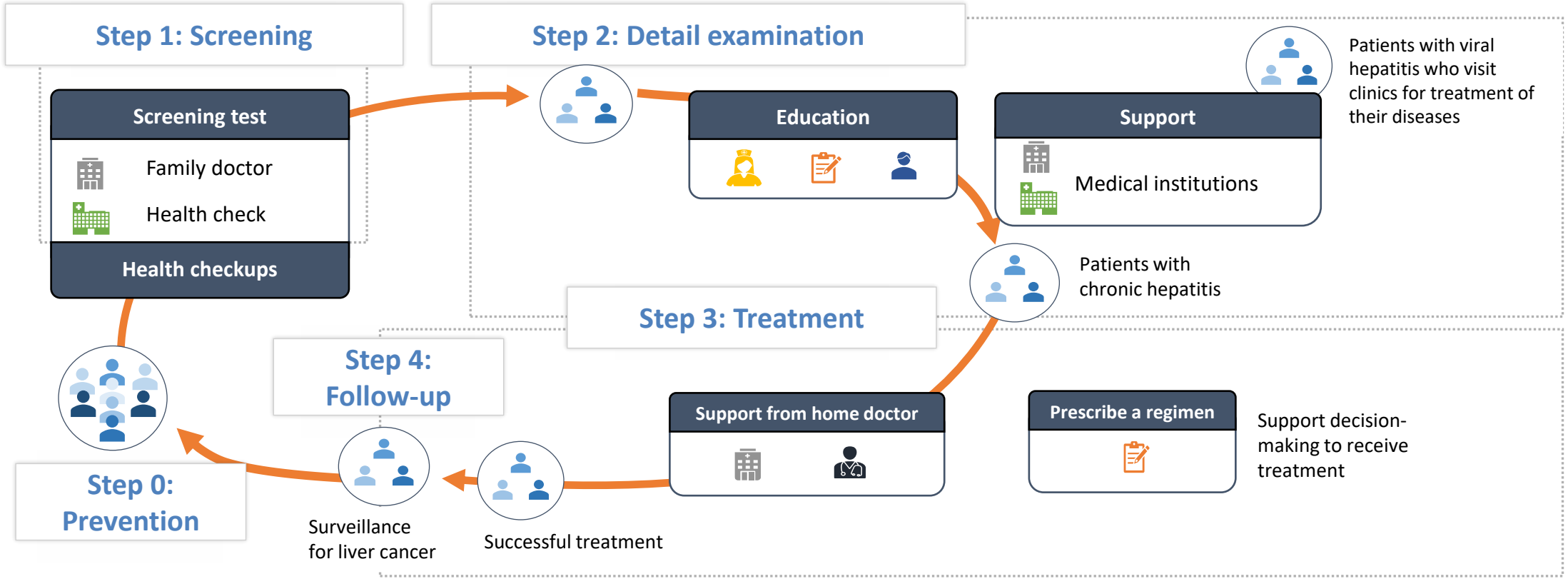
HBV, hepatitis B virus; IFN, interferon; FU, follow-up; M, million; PHC, primary healthcare clinic.

1. Kanto T. *Glob Health Med* 2021;3:249 – 252. doi: 10.35772/ghm.2021.01078;
2. Ministry of Health, Labour and Welfare. Available at https://www.mhlw.go.jp/content/10901000/000487984.pdf (Accessed March 4, 2022)

Ministry of Health, Labour and Welfare

Hepatitis medical care coordinators

- A key player in supporting test, treat and care for hepatitis patients

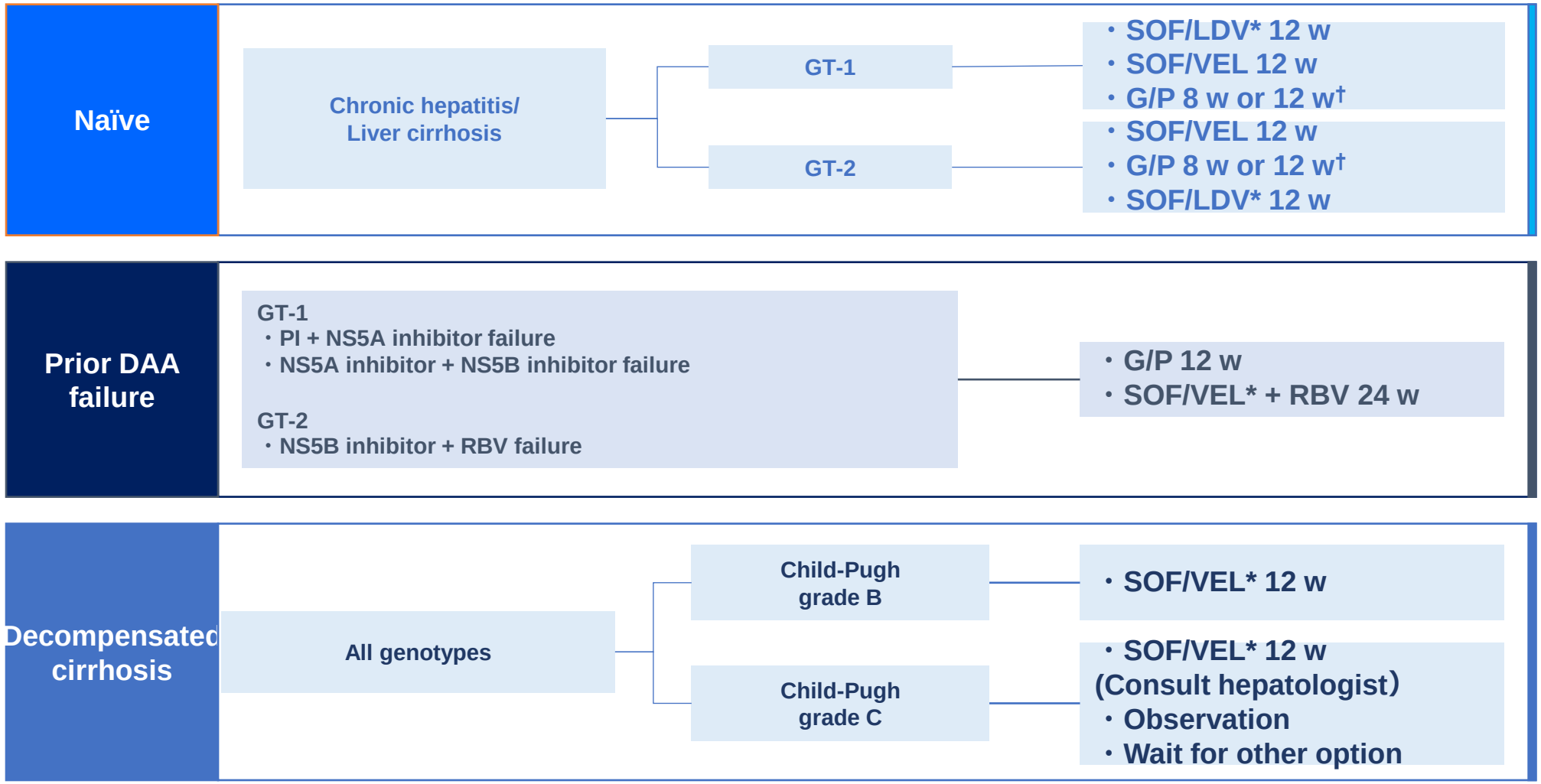


Various personnel are expected to play supportive roles for patients accepting proper services from healthcare systems and governments

Public health nurses | Patients group | Government officer | Workplace officer | Nurses | Doctors | Dentists | Pharmacists

Isoda H, et al. Glob Health Med 2021;3:343–50.

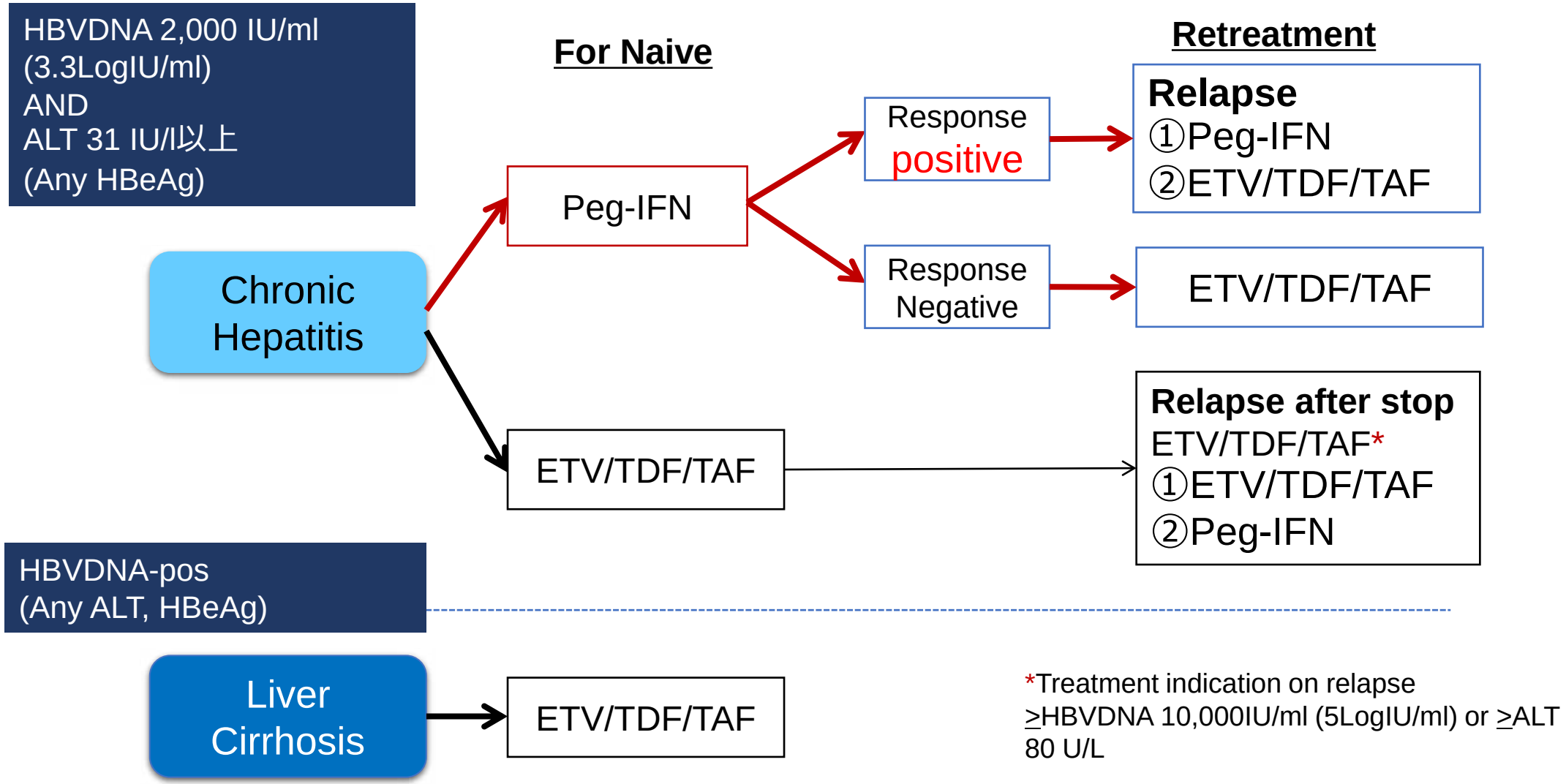
Japan Society of Hepatology guidelines for HCV therapy, updated 2024



*SOF is contraindicated in patients with severe renal impairment (eGFR <30mL/min/1.73m^2) or renal failure requiring dialysis; †8 w in patients with chronic hepatitis and 12 w in patients with liver cirrhosis.
DAA, direct-acting antiviral; EBR, elbasvir; EBR, elbasvir; eGFR, estimated glomerular filtration rate; G/P, glecaprevir/pibrentasvir; GT, genotype; GZR, grazoprevir; LDV, ledipasvir; PI, protease inhibitor; RBV, ribavirin; SOF, sofosbuvir; VEL, velpatasvir; w, weeks.

Adapted from, Japan Society of Hepatology. Hepatology Res 2020;50:791–816.

Japan Society of Hepatology guidelines for HBV therapy, updated 2022

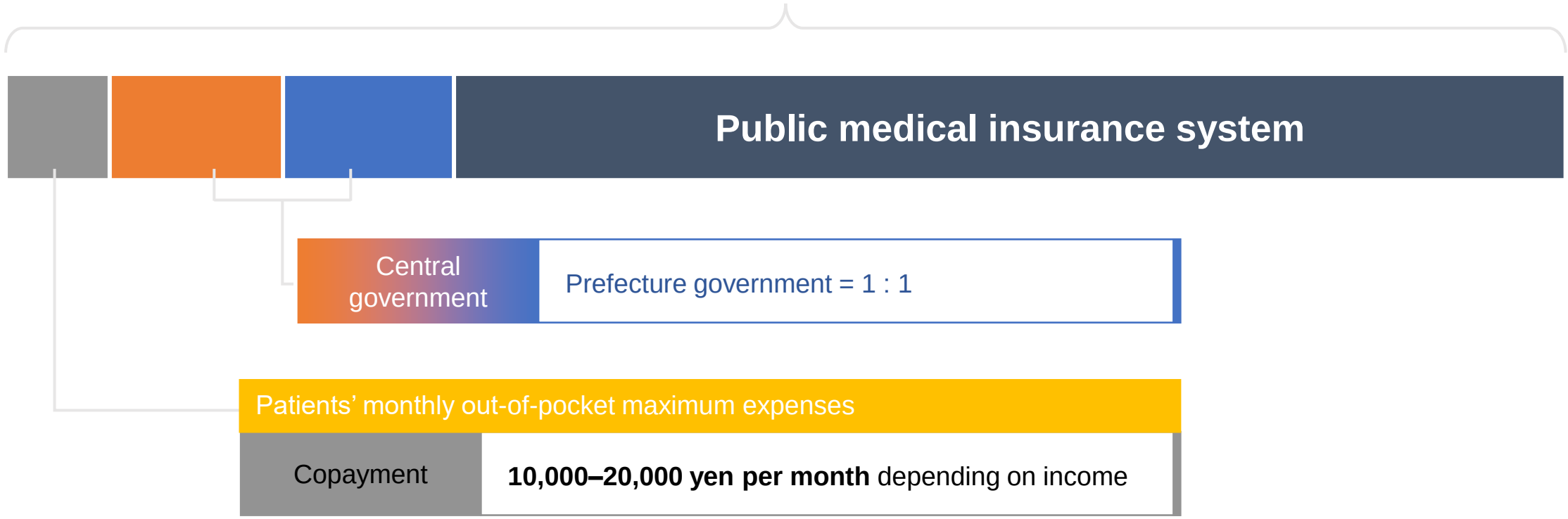


*Treatment indication on relapse
≥HBVDNA 10,000IU/ml (5LogIU/ml) or ≥ALT 80 U/L

Adapted from, Japan Society of Hepatology Clinical GL for HBV

Subsidy program for the coverage of cost for hepatitis treatments in Japan

Medical expenses

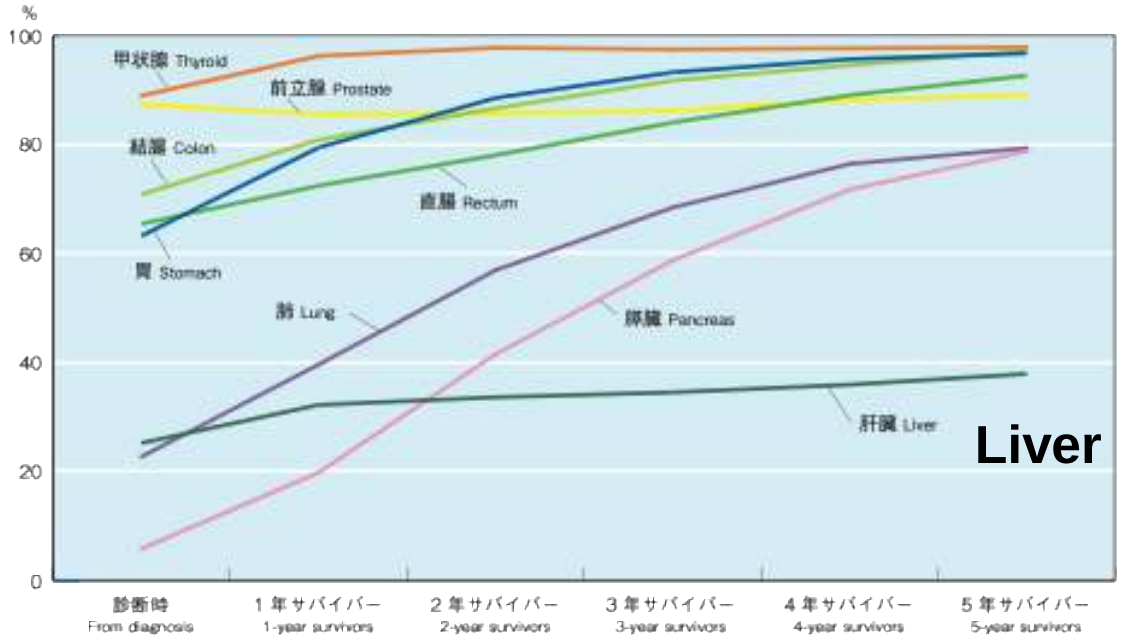


Oza N, Kanto T, et al. Hepatol Res 2017: 47: 487-496.

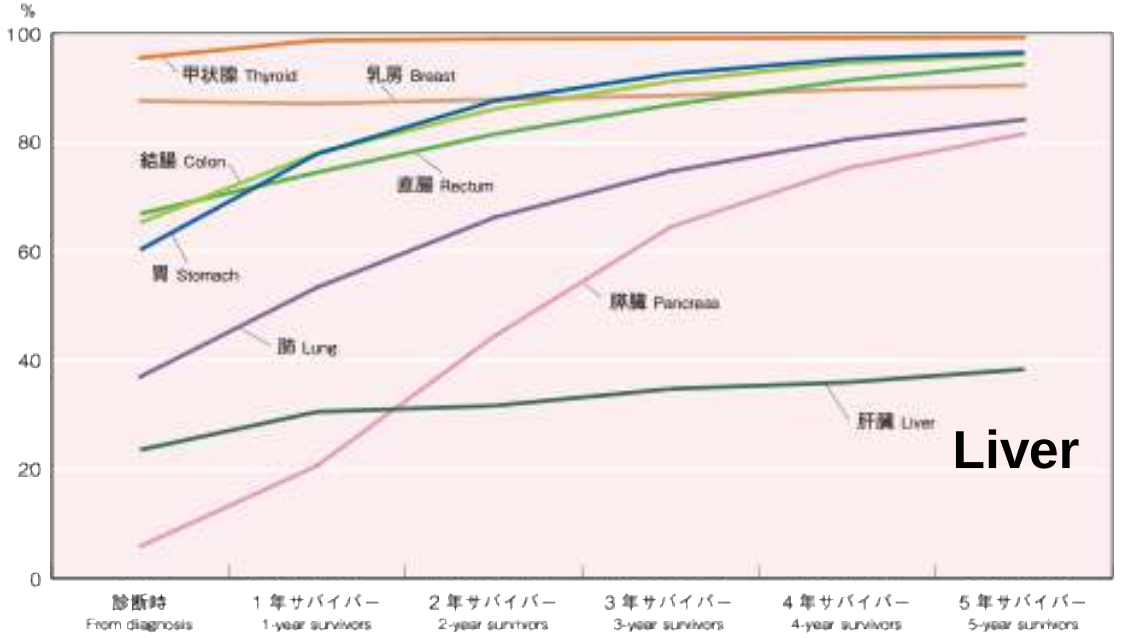
Conditioned 5-year survival rate in various cancers in Japan (2002 – 2006)

Population-based cancer registries, Period method

Male aged 15-99 yrs.

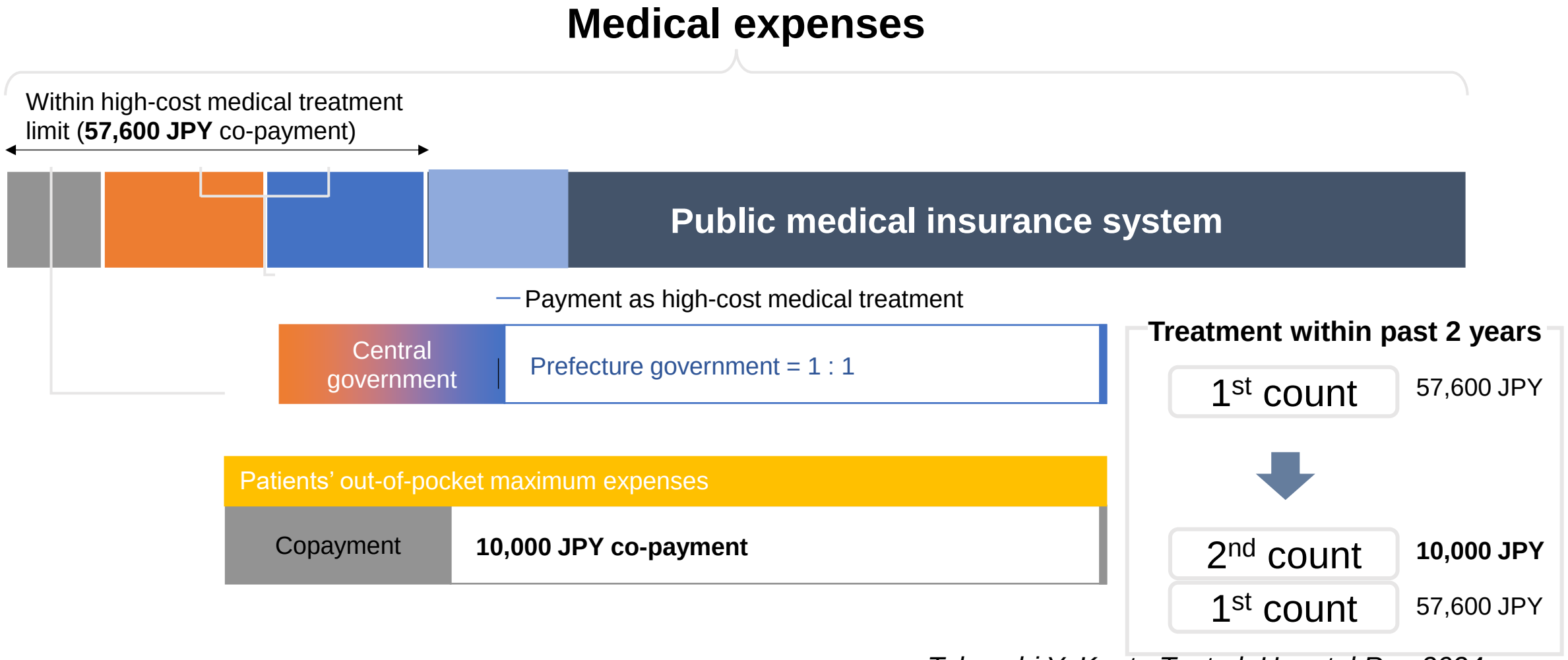


Female aged 15-99 yrs.



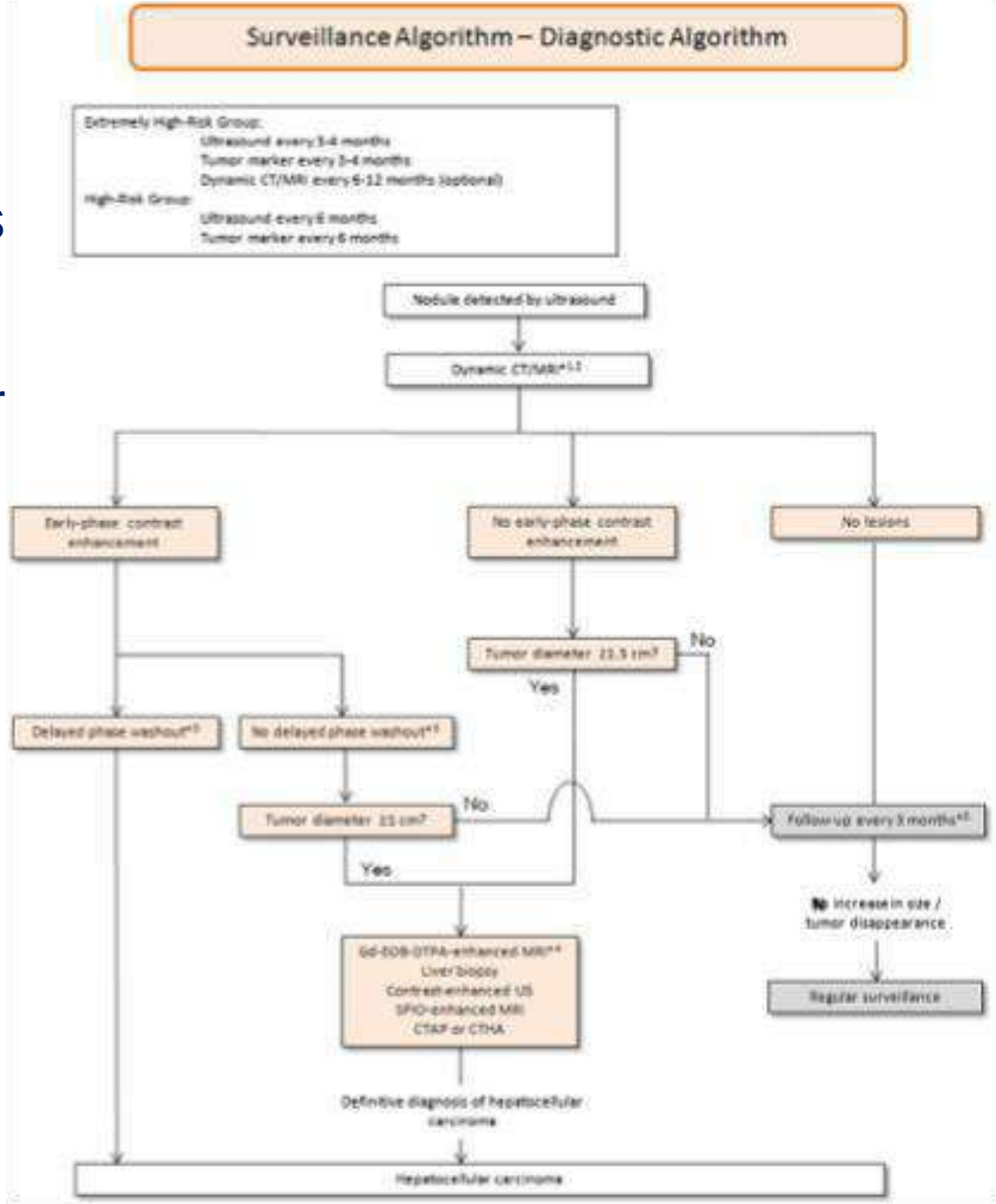
Foundation for Promotion of Cancer Research, Cancer statistics in Japan 2022.

Subsidy program for the coverage of cost for HCC or decompensated cirrhosis repetitive treatments in Japan



Takeuchi Y, Kanto T, et al. Hepatol Res 2024

Algorithm for surveillance and diagnosis in the 4th JSH-HCC Guidelines for HCC



High risk group:

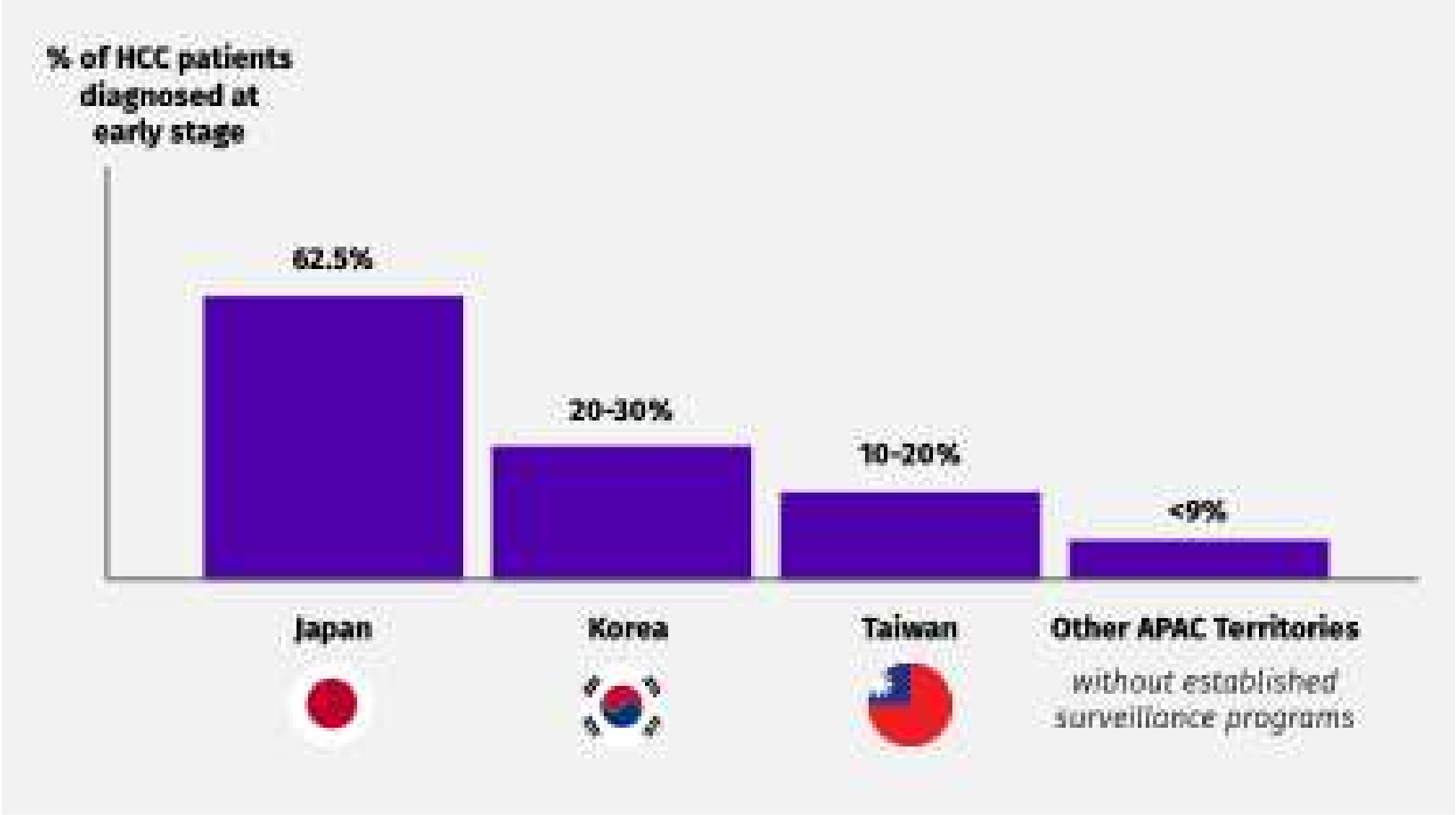
- Cirrhosis
- Chronic hepatitis B
- Chronic hepatitis C
  →US* + TM# every 6 months

Extremely high-risk group:

- Cirrhosis type B
- Cirrhosis type C
  →US + TM every 3-4 months
  →Dynamic CT/MRI every 6-12 months (optional)

*US: ultrasonography
#TM: tumor markers, AFP, PIVKA-II, AFP-L3

Diagnosis rate of HCC patients at early stages (BCLC 0 or A) in Japan

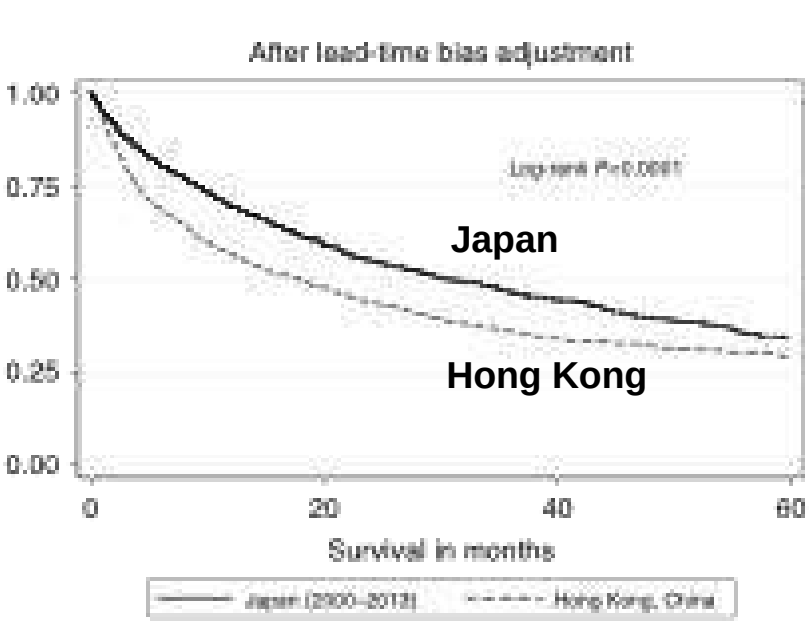


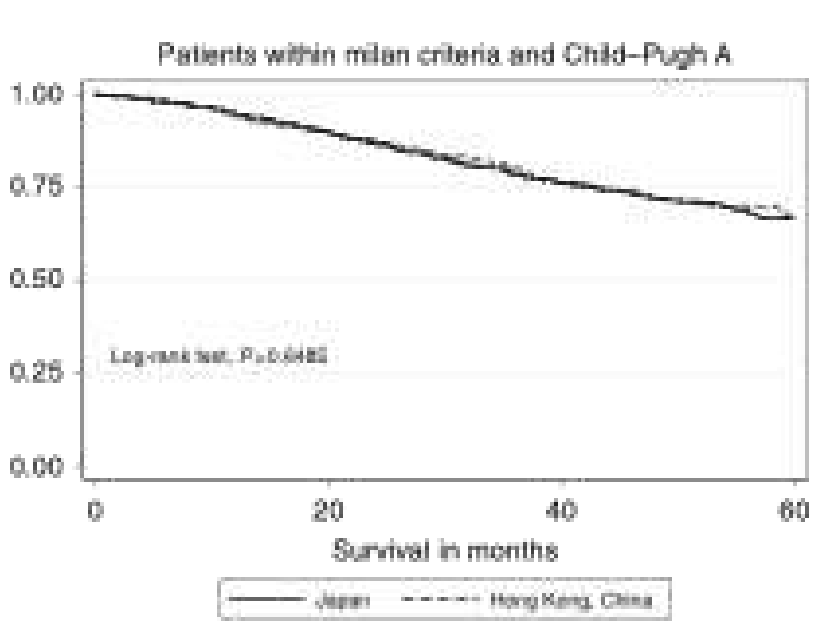
In APAC HCC white paper 2024, adapted from Kudo M. Liver Cancer 2015;4:39-50

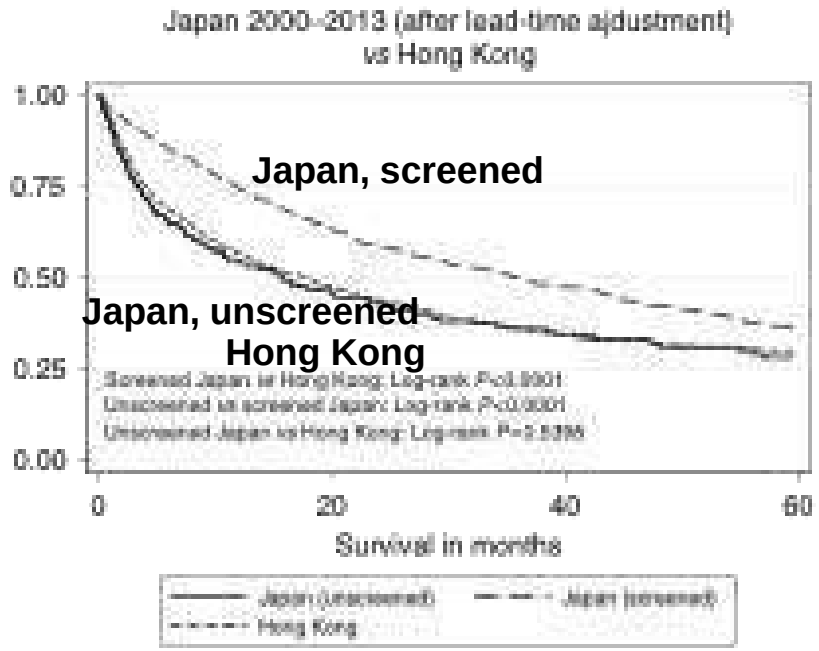
Impact of surveillance on early diagnosis and survival of patients with HCC

Japan cohort: N=1,174 (2000-2013)
- Intensive national surveillance program
- **75%** cases detected by surveillance,
- **62%** diagnosed at early stages,
- **63%** received curative treatment

Hong Kong cohort: N=1,675 (2003-2014)
- No surveillance
- **<20%** cases detected pre-symptomatically,
- **32%** diagnosed at early stages,
- **44%** received curative treatment

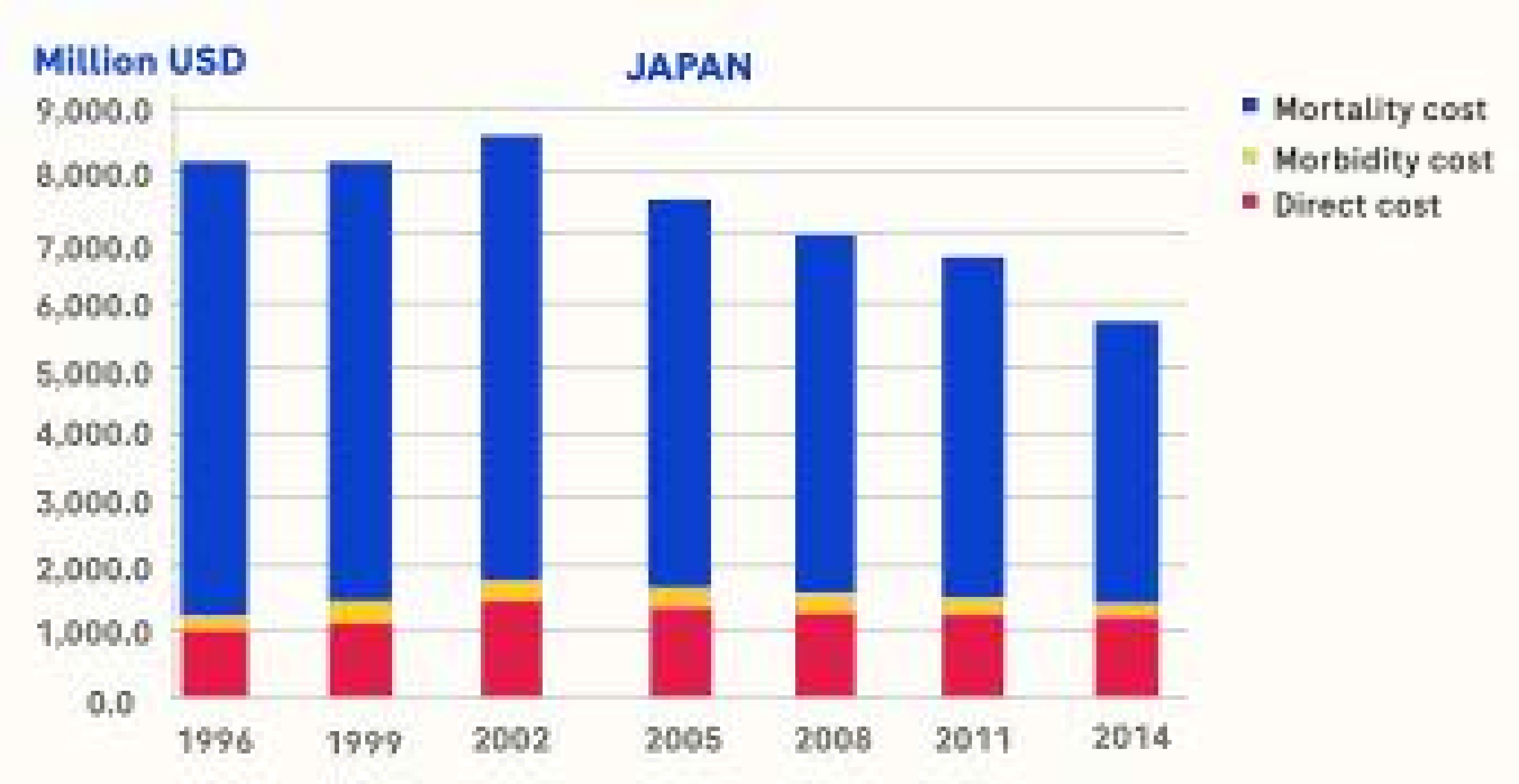






Johnson P, et al. Br J Cancer 2017;116:441-447

Trend of cost of illness of primary liver cancer per capita in Japan



In Diagram 2024;14 adapted from Wu Y, et al. Health Economics Review 2020,10:38

Summary

- In Japan, **Basic Act on Hepatitis Measures** was enacted in 2009, which has been promoting comprehensive hepatitis measures in screening, treatment, and care for patients with viral hepatitis.
- Anti-HCV and anti-HBV treatment is **optimized** for patients according to the conditions of liver disease, the cost of which are covered by medical insurance and **special subsidy program for viral hepatitis** in Japan.
- In Japan, a **surveillance system for liver cance**r has been established, early-stage liver cancer is being diagnosed, and deaths from liver cancer are decreasing.
- In order to support the repetitive treatment of liver cancer, there is a **subsidy program for second and subsequent liver cancer treatments**.
- To encourage testing and treatment, specialized health care workers, **hepatitis medical coordinators**, have started to support patients in need.
- In collaboration with liver societies in Asian countries, **JSH is actively involved in the fight against viral hepatitis and liver cancer.**

APAC Hepatocellular Carcinoma Policy Forum 2024

Bangkok October 2, 2024

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

Clinical and economic burden of HCC in APAC

Urgent call for enhanced recognition, national plans and patient journey insights

Mr. Will Brown
Senior Director, Vista Health

APAC Liver Disease Alliance

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

There is an urgent need to address hepatocellular carcinoma in Asia Pacific

Hepatocellular carcinoma (HCC) is the most common type of liver cancer

In Asia Pacific, HCC is also the

- **5th most common cancer**
- **2nd deadliest cancer**

Accounting for

72%

of HCC deaths worldwide

In Asia Pacific, hepatitis B and C are the

top causes

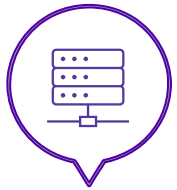
of cirrhosis-related and liver cancer-related deaths

USD 11.1 billion

economic burden of HCC, equivalent to 0.05% of the GDP, projected to increase to USD 34 billion by 2030

Sources: IARC, Asian Scientist, Global Burden of Disease, Lancet Gastroenterology and Hepatology (full sources in White Paper)

The white paper was the culmination of extensive literature review and collaboration with leading hepatitis and hepatocellular carcinoma experts

1. Targeted literature review

International and national sources in journal publications and symposiums such as the Hepatitis C Virus Elimination Symposium and Solidarity for Hepatitis Elimination

2. Information organization

Information gathered was organized into 3 themes:

1) the need to address hepatitis and HCC together
2) progress made and gaps in efforts to tackle hepatitis and HCC
3) best practices from successful case studies

3. Engaging key opinion leaders

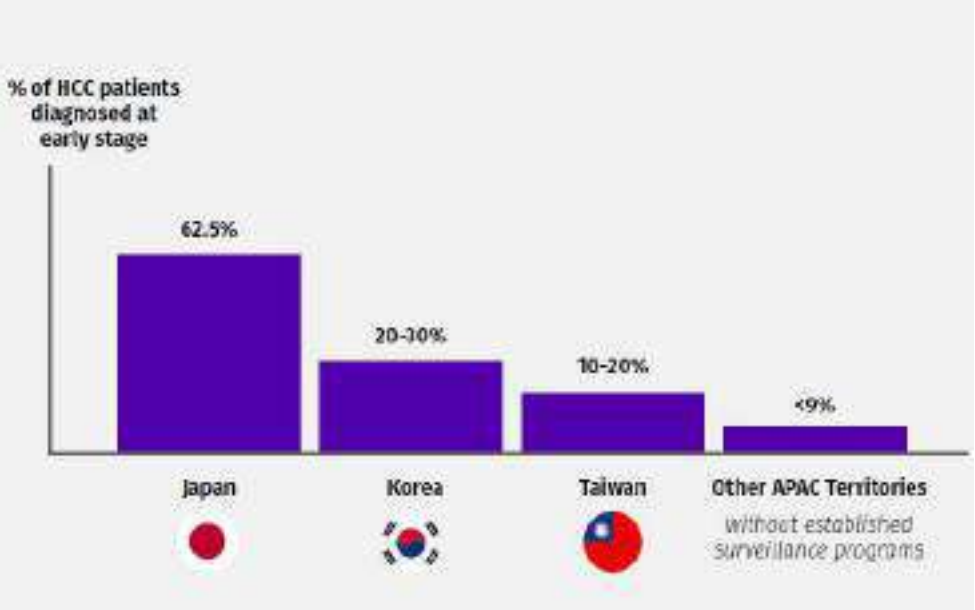
Insights and recommendations in the white paper were developed and refined through the collaborative efforts of leading hepatitis and HCC experts in Asia.

4. White paper

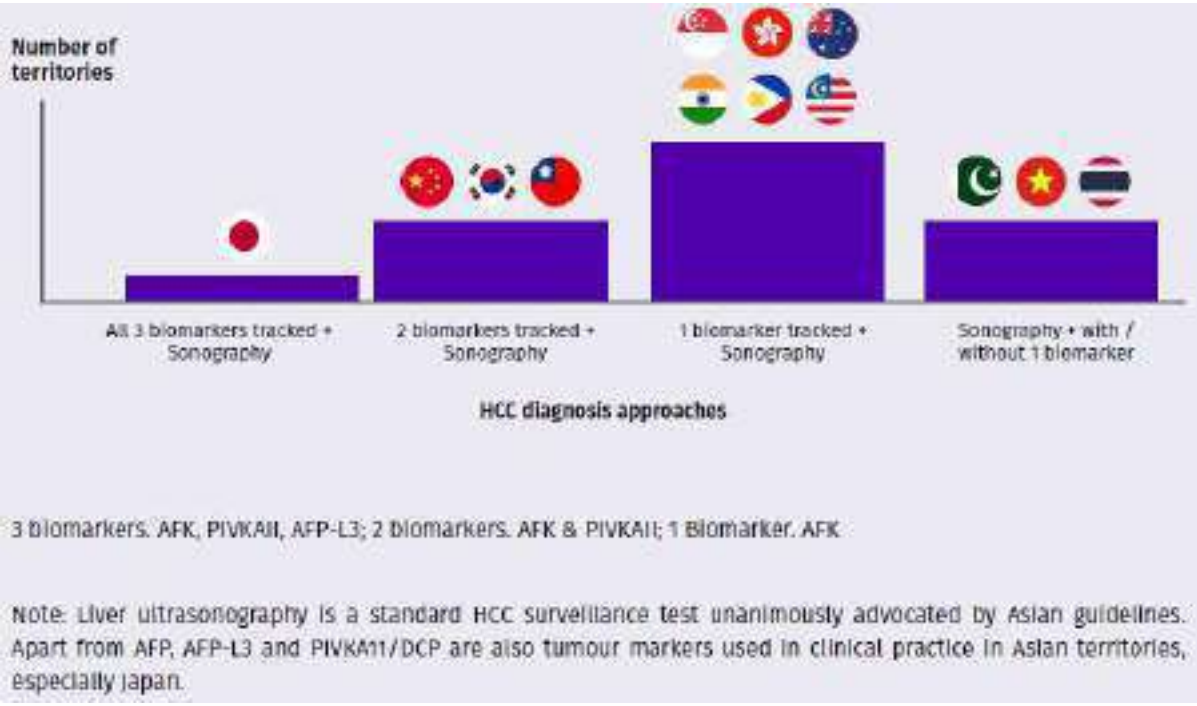
The white paper aims to galvanize hepatitis elimination and HCC control efforts in Asia at regional and national levels.

There is a stark disparity in patient journey in the region; much can be learned from Japan's approach

NATIONAL SURVEILLANCE PROGRAM IS ASSOCIATED WITH EARLIER DETECTION OF HCC & LONGER SURVIVAL



HCC SURVEILLANCE CAN BE OPTIMIZED BY IMPLEMENTING A NATIONAL SURVEILLANCE PROGRAM THAT USES ULTRASOUND AND 3 TUMOUR MARKERS



Source: Kudo M. Management of Hepatocellular Carcinoma in Japan as a World-Leading Model. Liver Cancer. 2018;7(2):134-147. doi:10.1159/000484619

Japan has established its position as the world's best HCC practice system through their comprehensive approach across the following domains

Checklist of success factors in Japan

Early HCC detection due to established nationwide surveillance

- Free and regular testing for HBsAg and HCV Ab for high-risk patients
- Insurance coverage for AFP, PIVKA-II, AFP-L3 tumor markers, and medical imaging tools for high-risk patients
- Annual HCC awareness campaigns organized by JSH

Antiviral therapy for hepatitis

- Coverage for Interferon, DAA, and nucleoside analogue treatments
- Special reimbursement programs for HBV or HCV patients' treatment and medical expenses.

Establishment of precise diagnostic algorithm of HCC

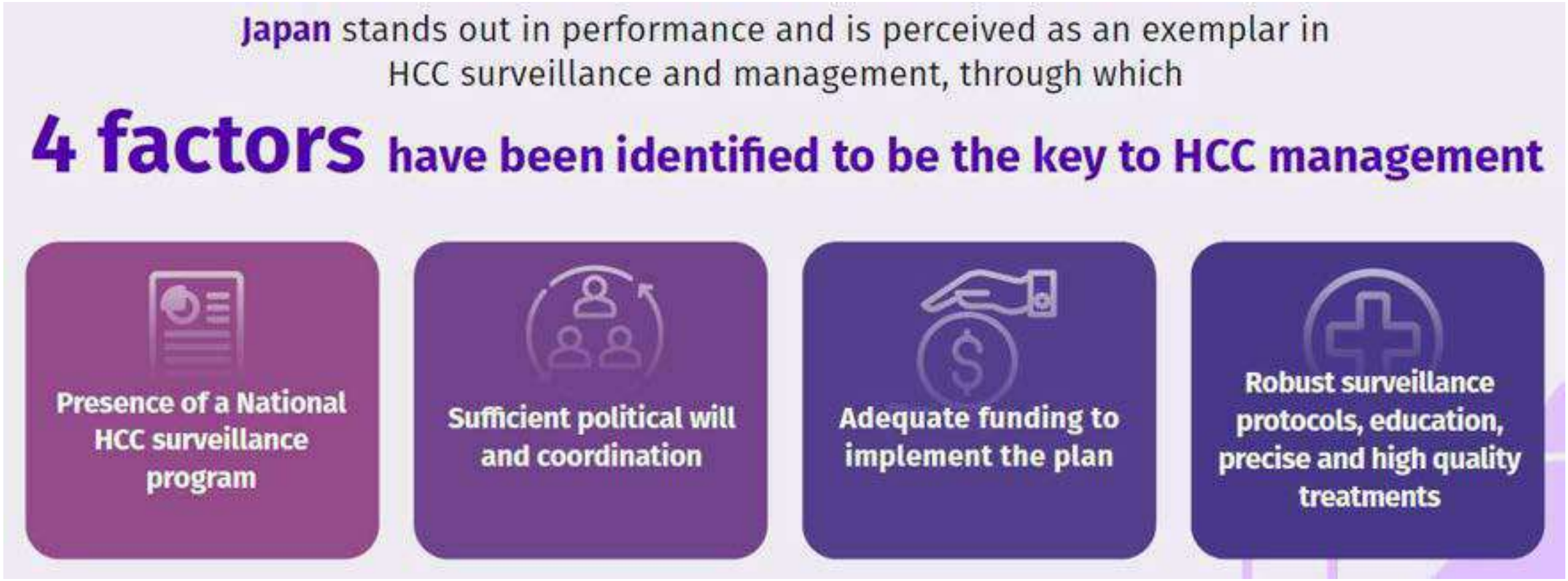
- Availability of advanced imaging techniques (CTHA/CTAP, CEUS)
- Extensive use of advanced imaging tools like EOB-MRI for improved detection
- Effective collaboration between pathologists and clinicians for image-pathology correlation

Precise & accurate treatment selection & high-quality treatment technique

- Superior treatment skills in resection, ablation, TACE, and HAIC techniques
- Comprehensive expertise of hepatologists in ablation, TACE, HAIC, and systemic therapy as organ specialists
- Multidisciplinary collaboration among all healthcare professionals

Source: Kudo M. Management of Hepatocellular Carcinoma in Japan as a World-Leading Model. Liver Cancer. 2018 May;7(2):134-147. doi: 10.1159/000484619. Epub 2017 Dec 13. PMID: 29888204; PMCID: PMC5985410.

The success story in Japan is a model for others in the region to follow

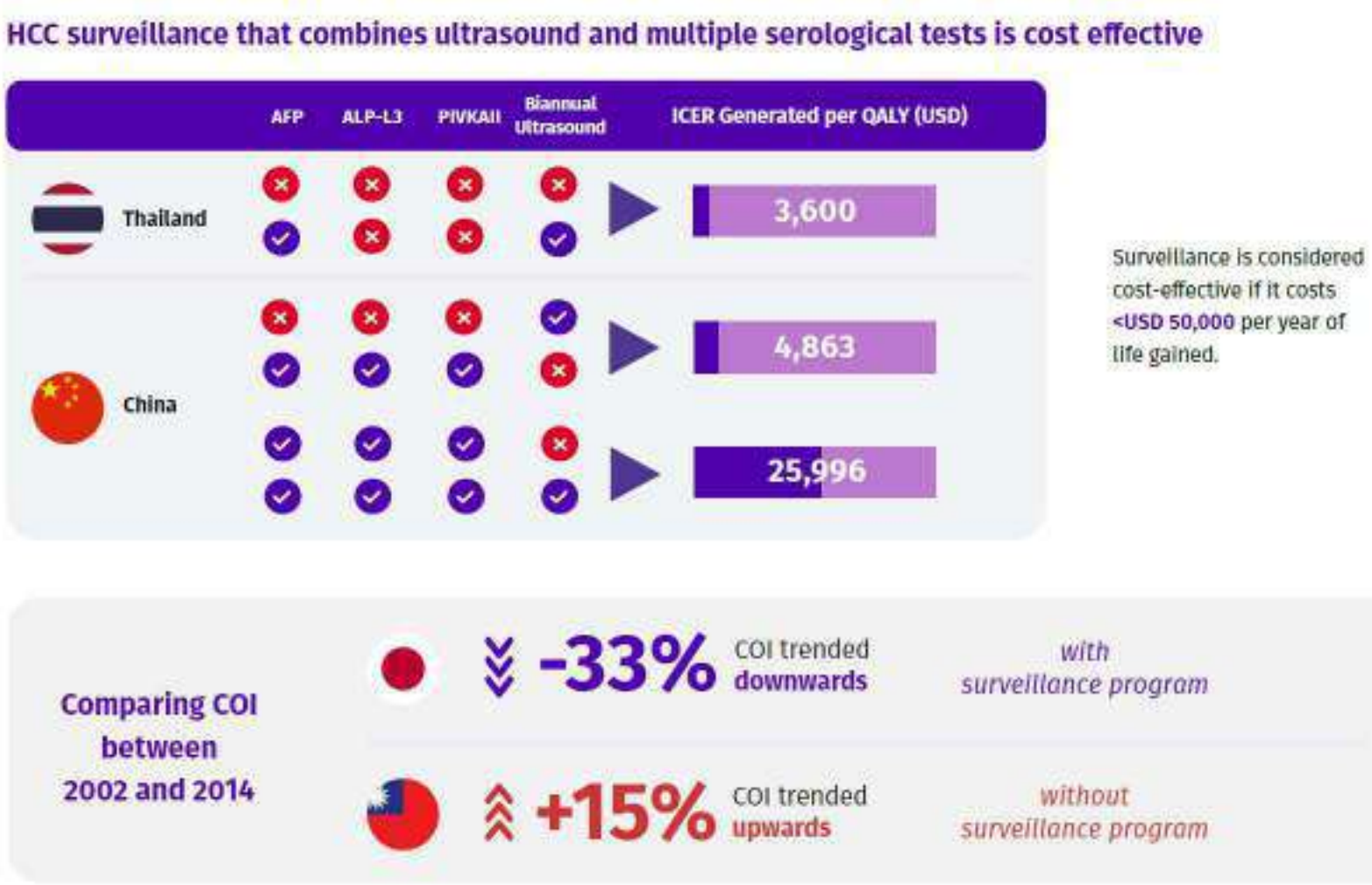


Source: Vista Health analysis

The White Paper lays out 5 policy recommendations to guide the Asia-Pacific response to hepatitis and hepatocellular carcinoma

Source: Vista Health analysis

Investing in a well-funded HCC surveillance program is crucial for effective management of the disease, offering significant cost-effectiveness



Sources: ISPOR, Health Economics Review (full sources in White Paper)

We believe each stakeholder in the healthcare ecosystem has something to offer, and something to gain

We call upon every stakeholder in the ecosystem, from Ministries of Health, policymakers and funders, industry and providers, or physicians, caregivers and patients to work together to ensure that the recommendations are implemented and tackle the problems faced.

Patients and their caregivers:
- De-stigmatization
- Improved access to screening, surveillance and treatment
- Chance of curing HCV
- Better prognosis for HBV and HCC

Healthcare professionals:
- Timely and appropriate clinical response
- Confidence in screening and diagnostic results

Governments and the economy:
- Healthier population → better economic productivity
- Reduce absenteeism due to debilitating symptoms associated with chronic HBV and late-stage HCC

Healthcare systems and payors:
- Progress towards UHC
- Increase cost-effectiveness by detecting and treating early
- Enhance economic efficiencies by integrating with existing health services
- Generate cost-effectiveness data using micro-elimination

Healthcare providers:
- Reduce operational costs and set-up time
- Alleviate bed crunch by detecting and treating patients early

Source: Vista Health analysis

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A Clinician's Perspective

Management of HCC in Japan as a world-leading model; best practices and lessons for other jurisdictions

Prof. Masatoshi Kudo
Professor & Chairman,
Department of Gastroenterology and Hepatology,
Kindai University Faculty of Medicine

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

A Clinician's Perspective Management of HCC in Japan as a World-leading Model

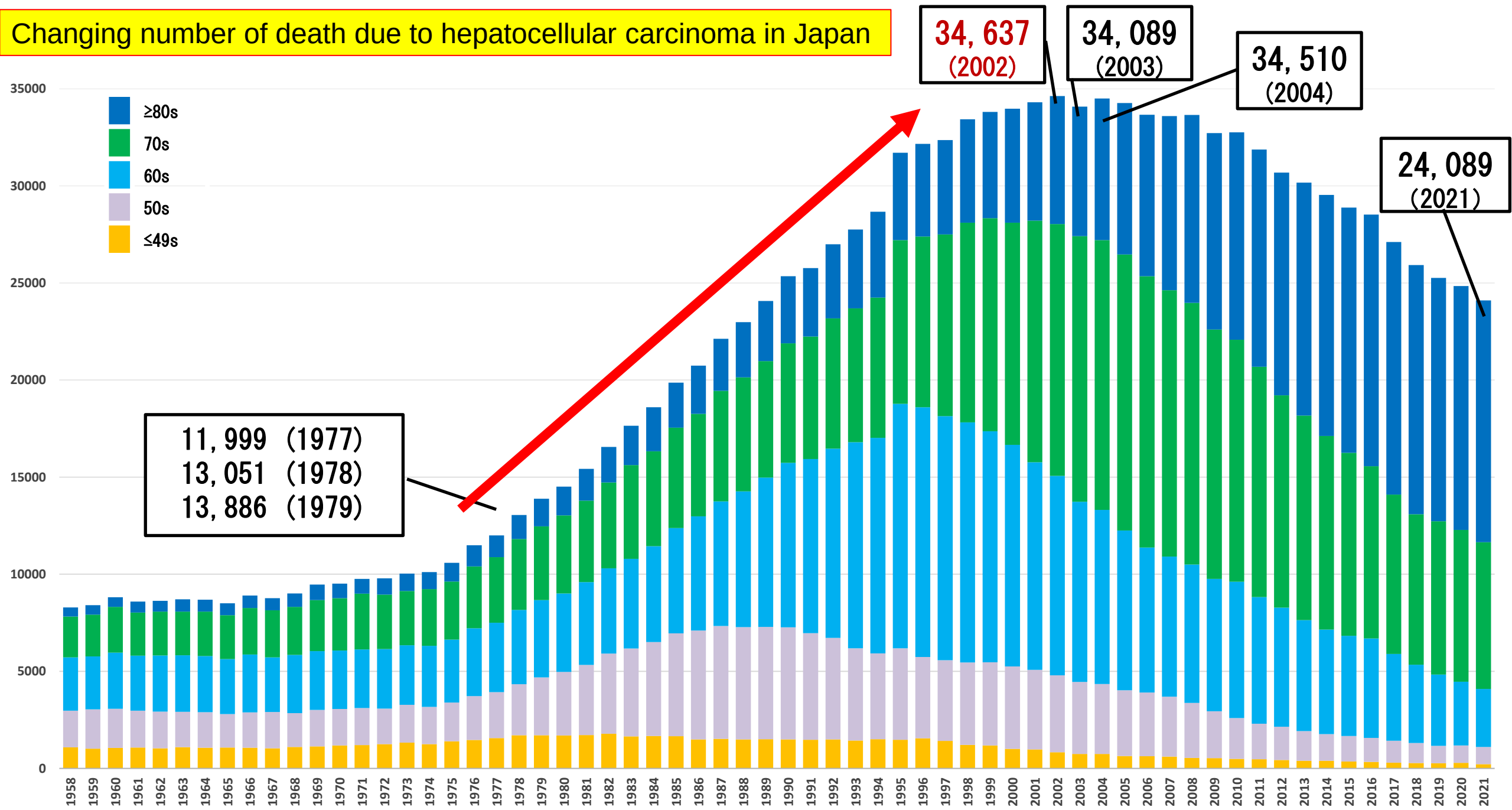
Best Practices and Lessons for other jurisdictions

Masatoshi Kudo, MD, PhD
Dept. of Gastroenterology and Hepatology
Kindai University Faculty of Medicine

Outline

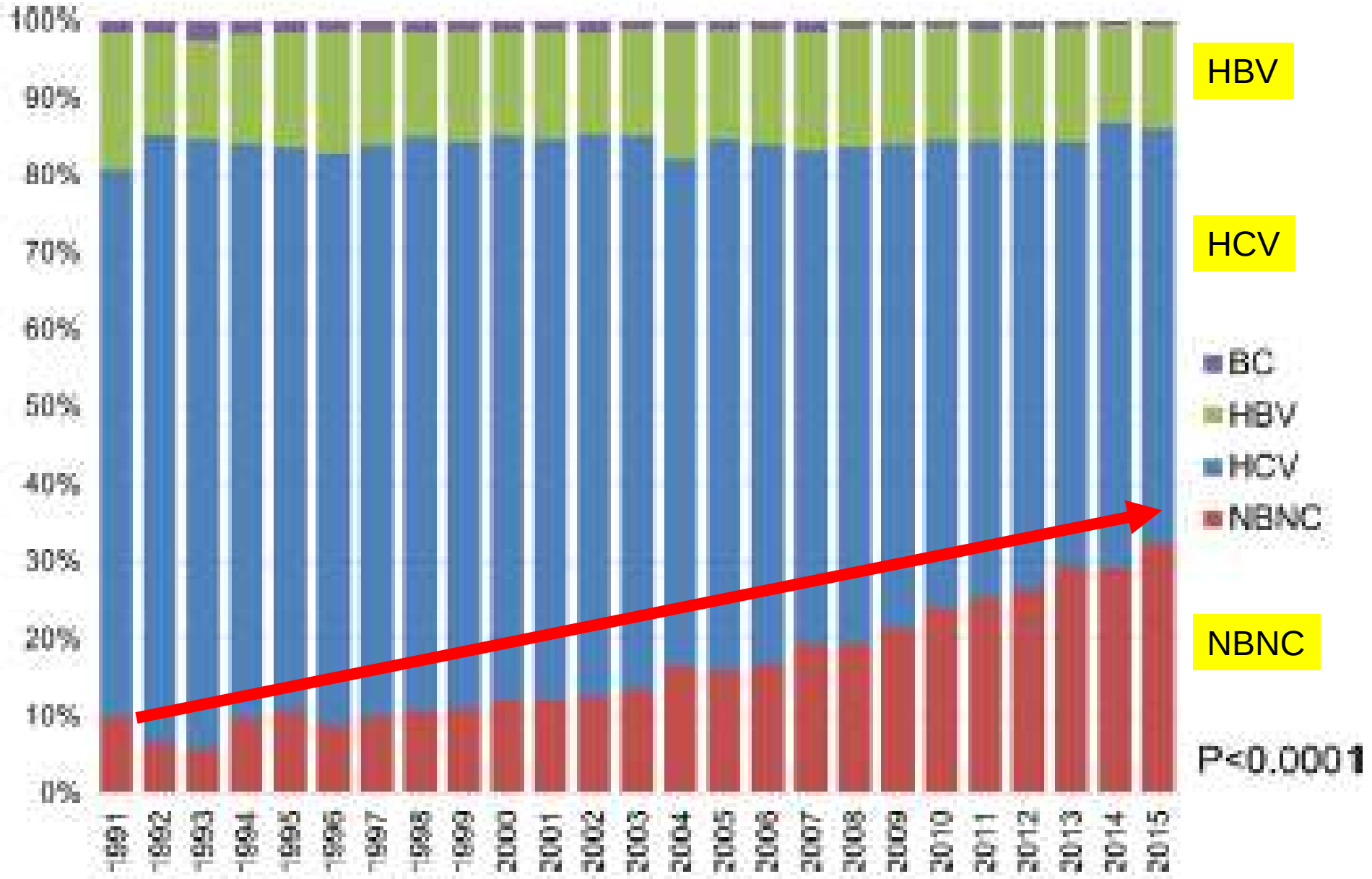
- Overview of HCC trend in Japan
- Overview of HCC outcome in Japan
- Overview of HCC surveillance in Japan
- Innovative treatment strategy in Early-stage HCC
- Innovative treatment strategy in Intermediate-stage HCC
- Innovative treatment strategy in Advanced stage HCC
- Role of Multidisciplinary Team
- Lessons learned from Japan’s experience
- Future innovations and Personalized Medicine

Changing number of death due to hepatocellular carcinoma in Japan



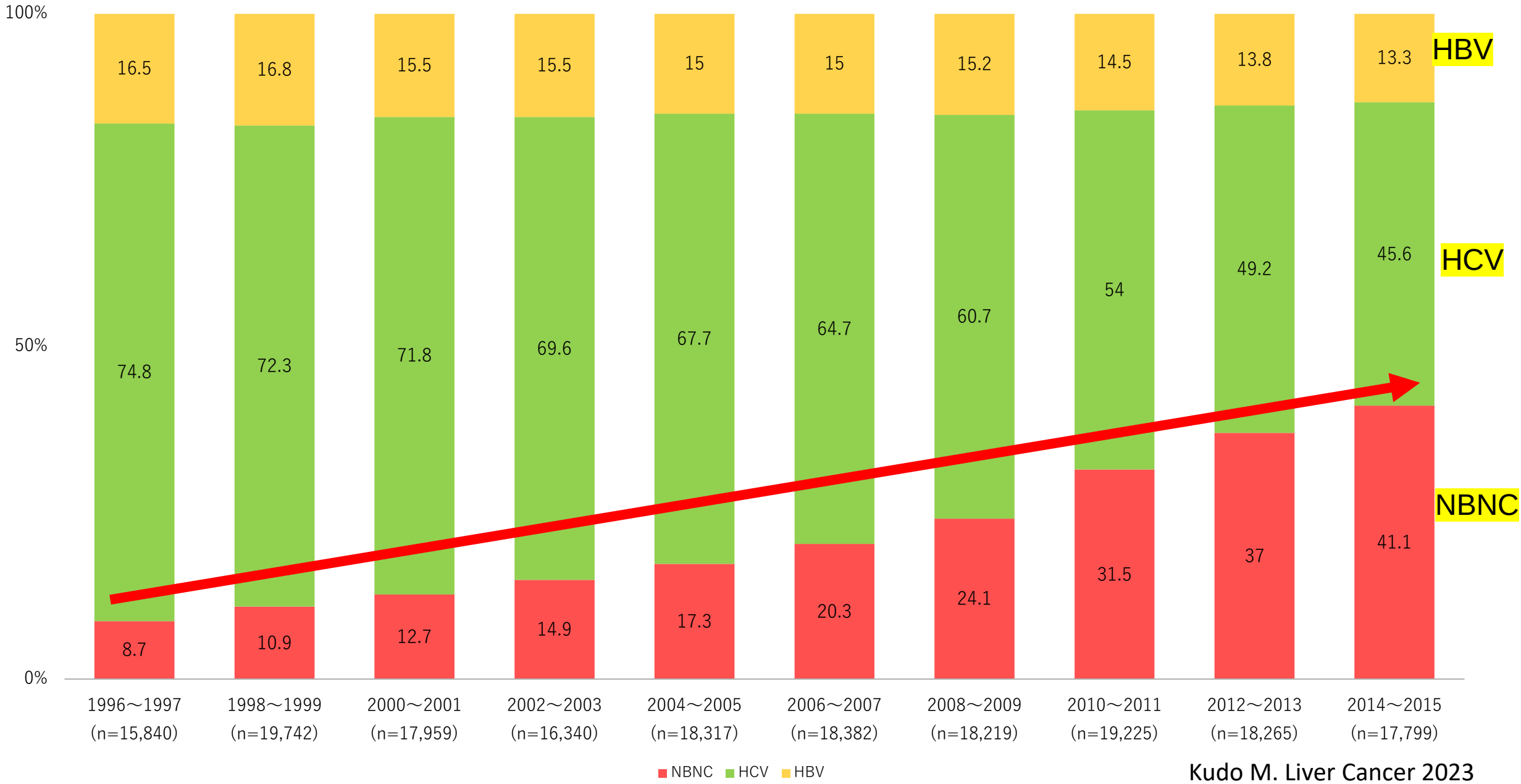
Citation from [National Cancer Center Japan] (https://ganjoho.jp/reg_stat/statistics/stat/cancer/8_liver.html)

Changing Etiology of HCC in Japan: Multicenter Study



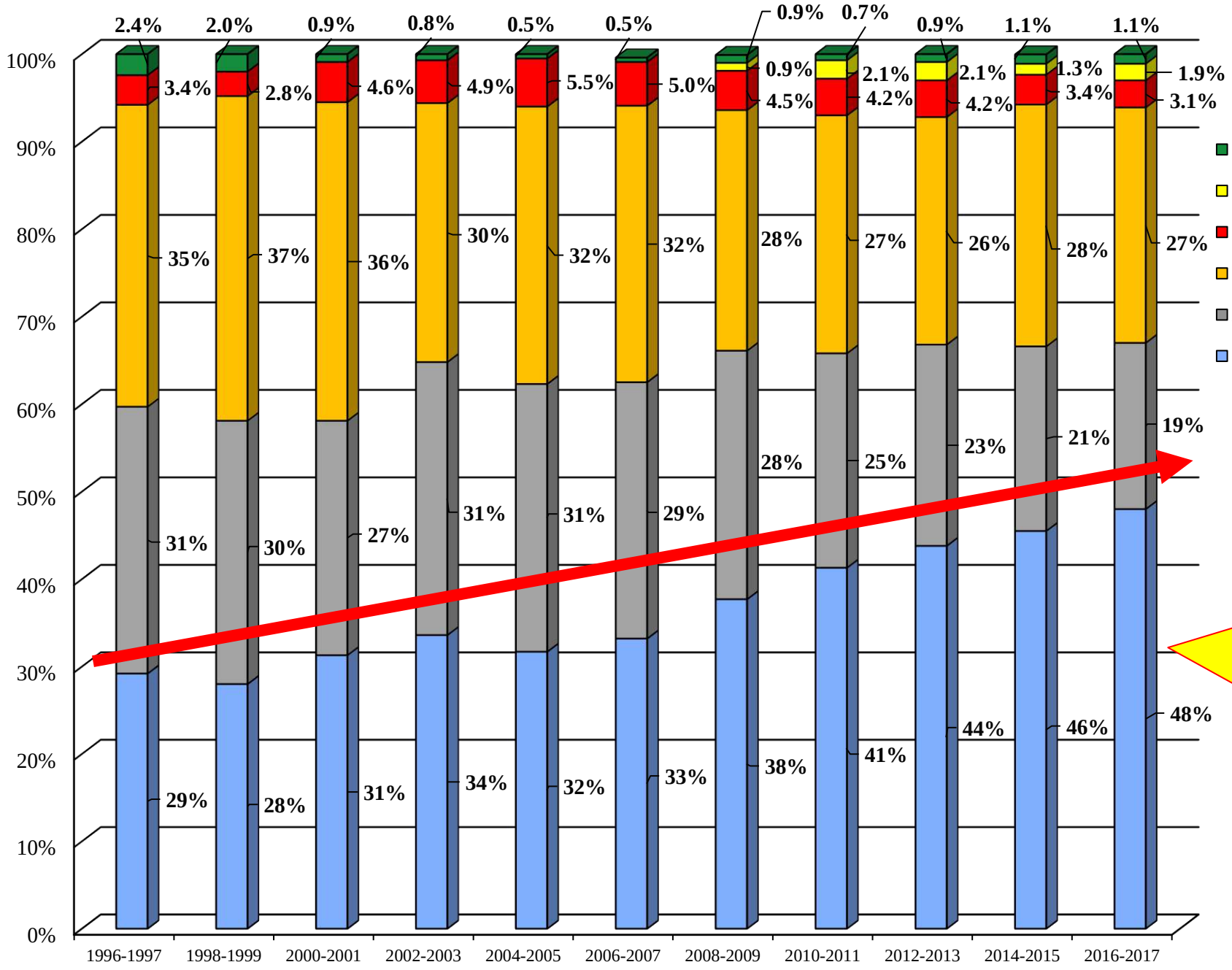
Tateishi R, et al. J Gastroenterol 2019

Changing Etiology of HCC in Japan: JLCA Nation-wide Follow-up Survey



Kudo M. Liver Cancer 2023

Initial Treatment Modality for Detected HCC: JLCA Nation-wide Follow-up Survey



Resection rate is increasing.

In surgical department, 60-70% of surgical patients with HCC are NASH/NAFLD etiology with mild fibrosis (**Huge tumor**)

Kudo M. Liver Cancer 2023

Outline

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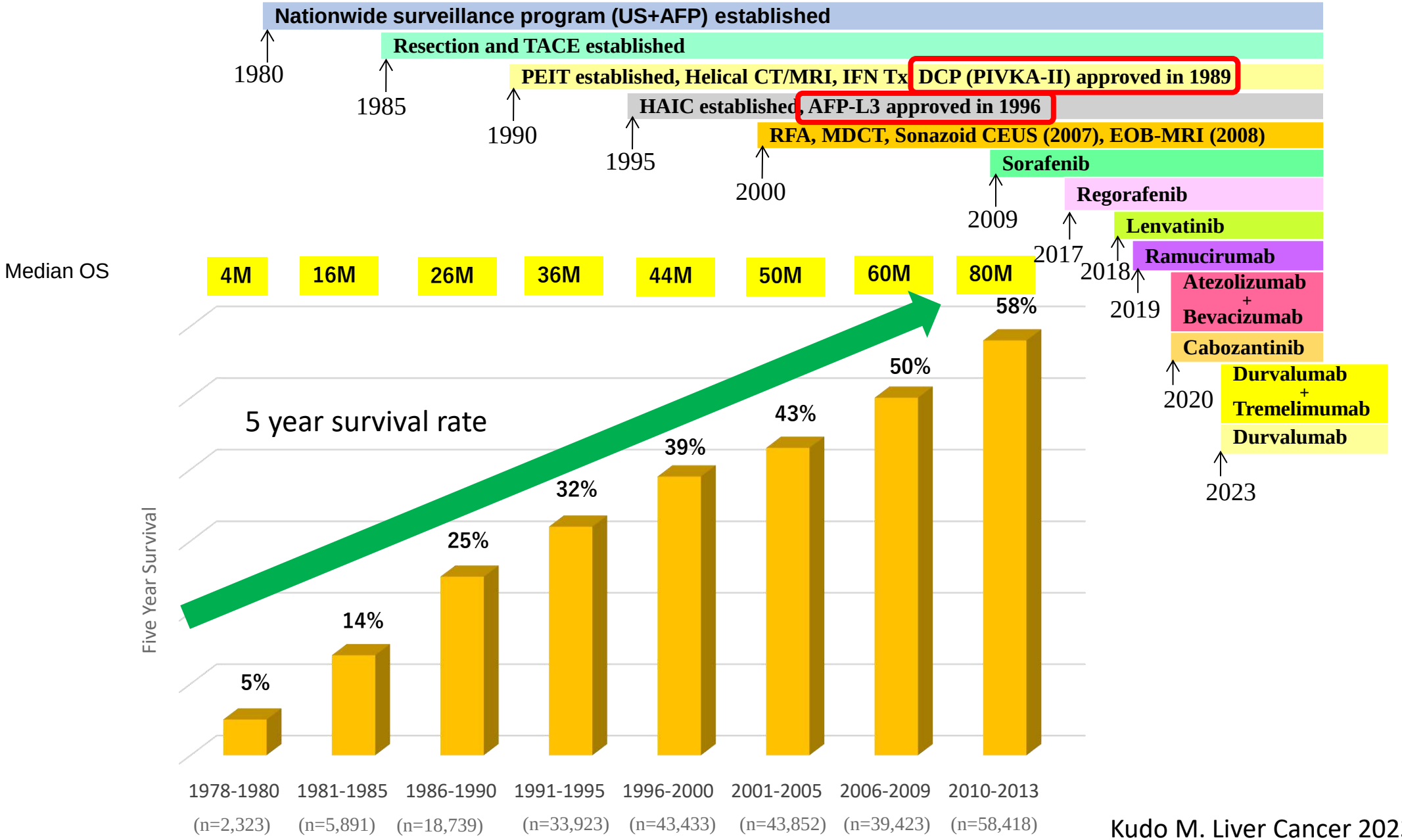
- Role of Multidisciplinary Team
- Lessons learned from Japan’s experience
- Future innovations and Personalized Medicine

Surveillance: Japan as a successful model

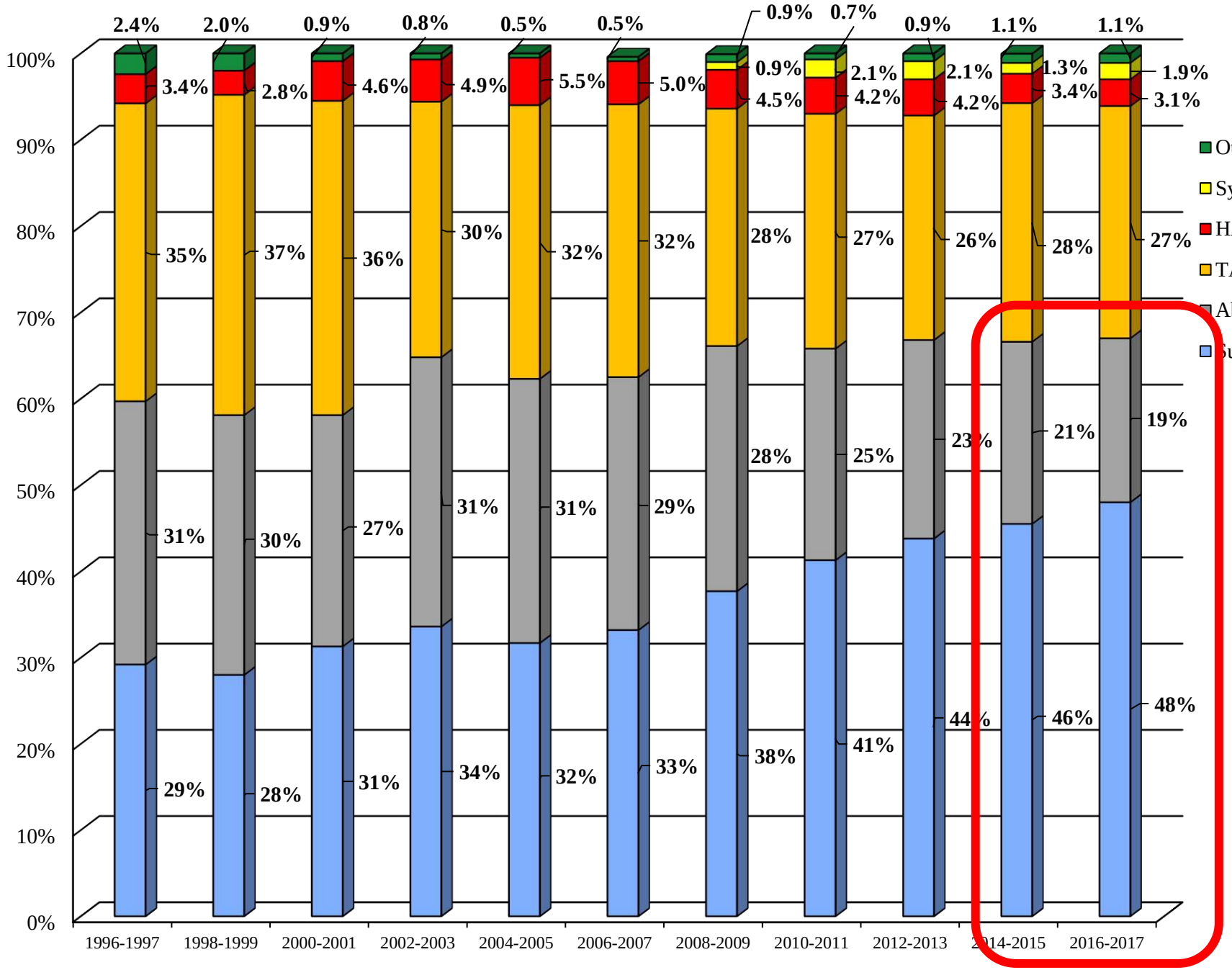
- Results of Nationwide Survellance of HCC by JLCA
- Regional Difference of OS Results According to GIDEON, Non-interventional study
- Treatment Outcome in Japan and Hong Kong: Effect of Nationwide Surveillance

Improvement 5 year survival rate and median OS in Japan in patients with all BCLC stage HCC



Kudo M. Liver Cancer 2023
24th Nation-wide Registry, JLCA

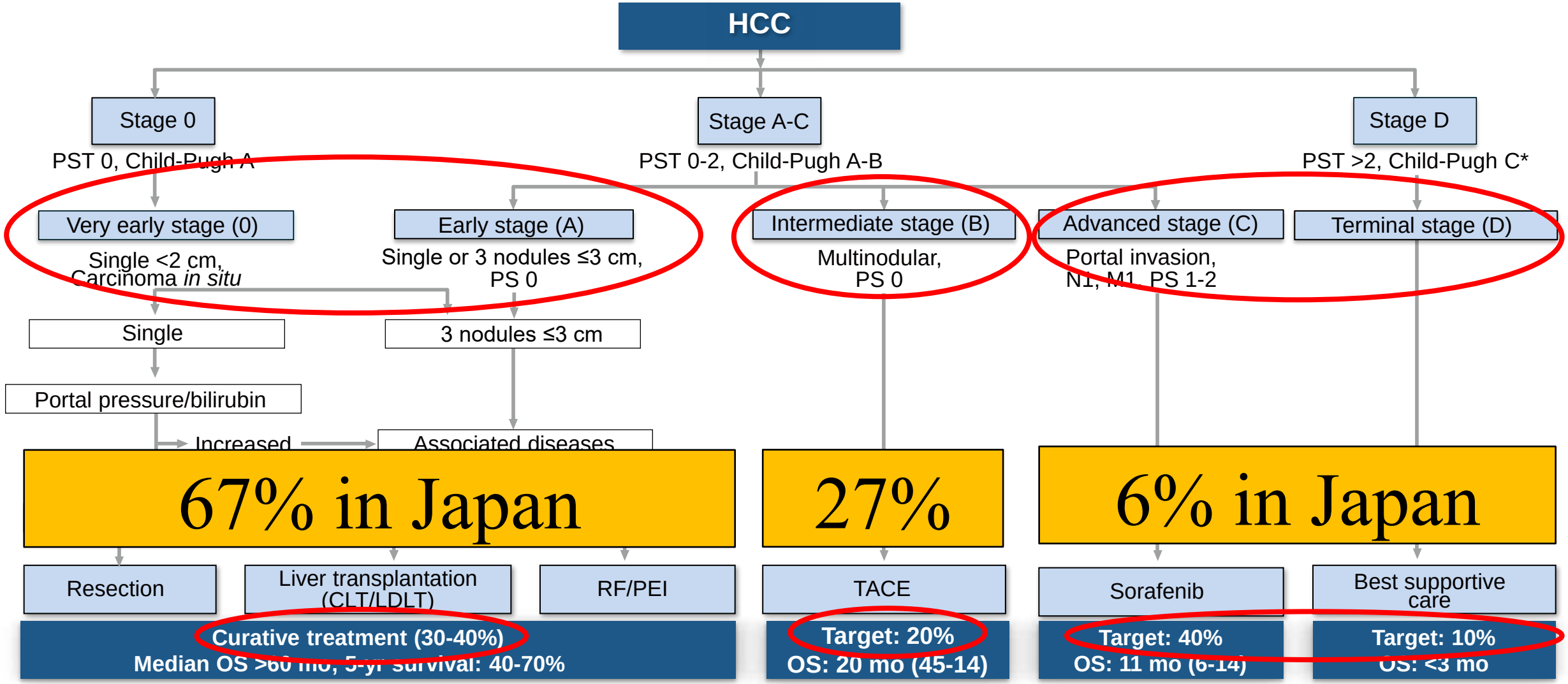
Initial Treatment Modality for Detected HCC: JLCA Nation-wide Registry Follow-up Survey



67% of patients received Curative therapy

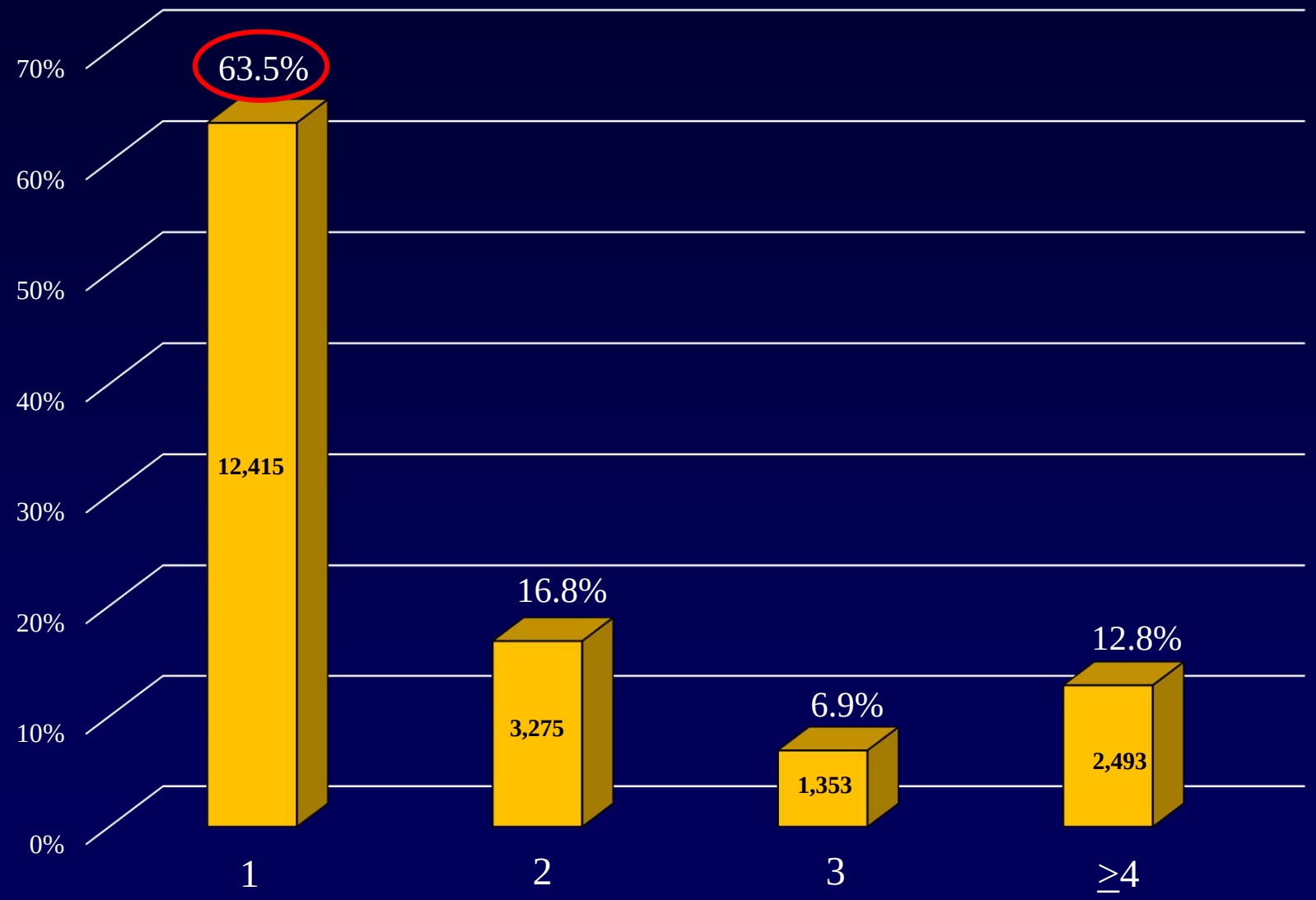
Kudo M. Liver Cancer 2023

BCLC/AASLD/EASL Staging and Treatment Algorithm



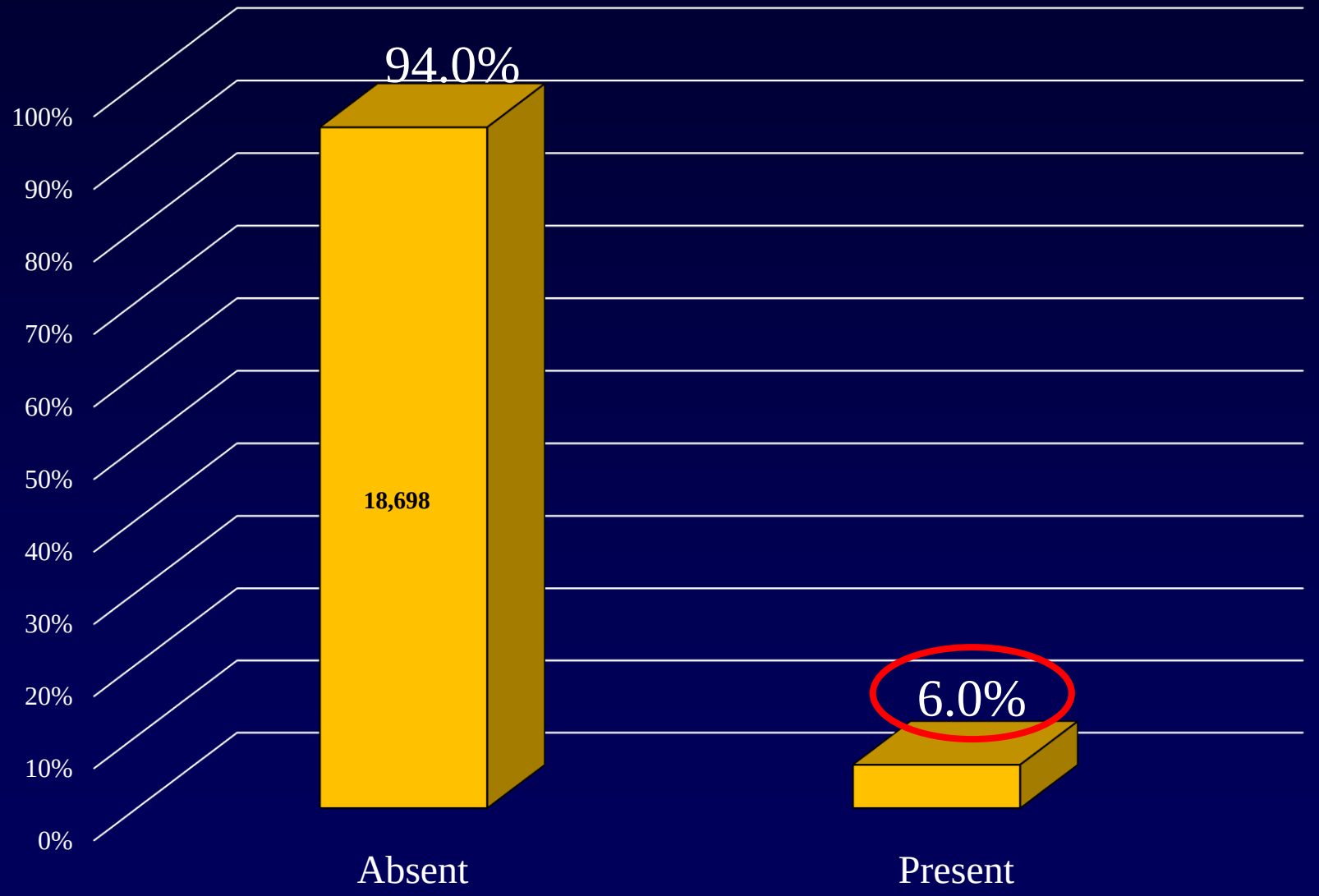
Bruix et al : Hepatology 2011 Mar;53(3):1020-2

Number of Nodules at the Time of Initial Detection (n=19,536)



21st Nation-wide Follow-up Survey, Japan Liver Cancer Association, 2020

Presence or Absence of Extrahepatic Spread at the Time of Initial Detection (n=19,887)



21st Nation-wide Follow-up Survey, Japan Liver Cancer Association, 2020

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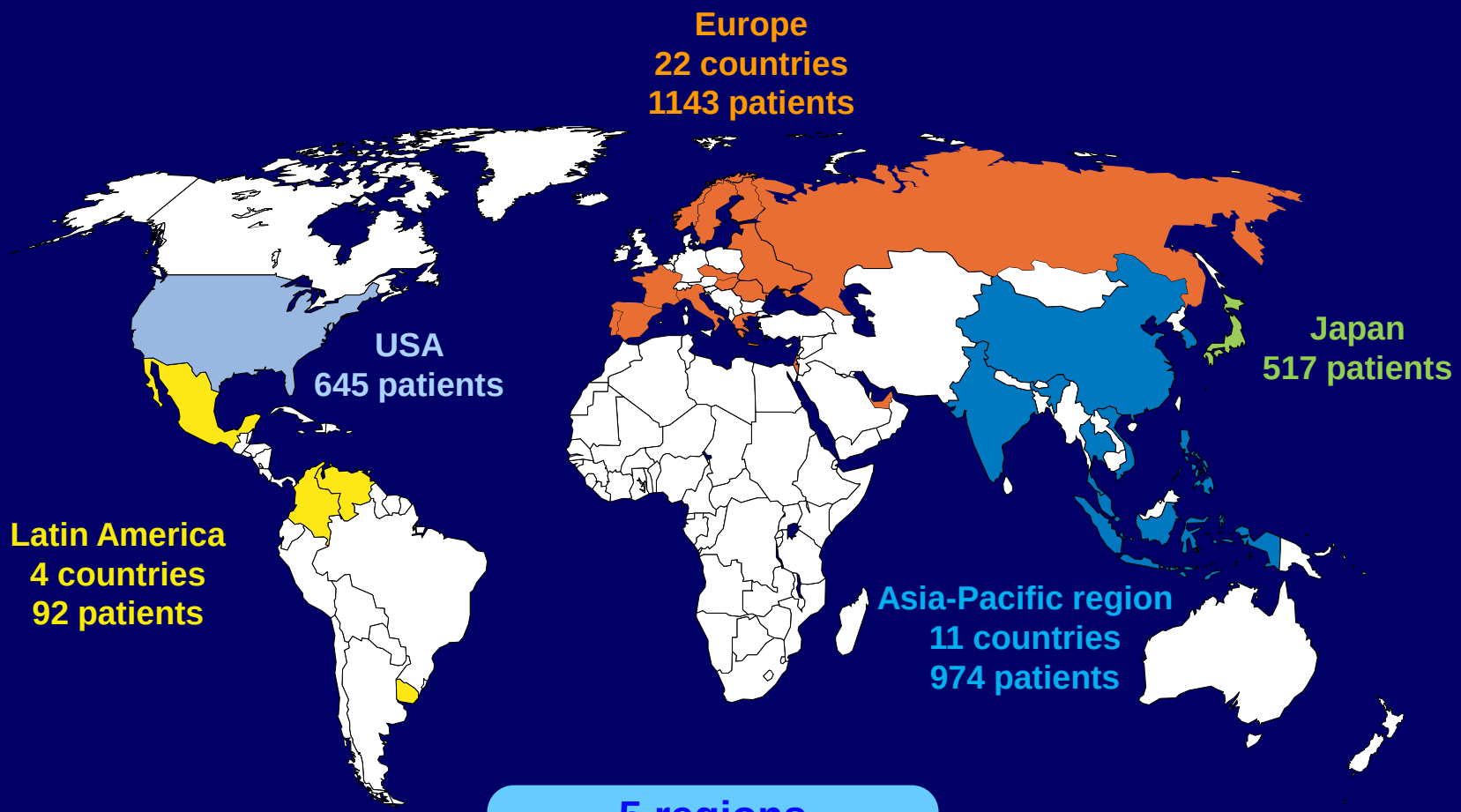
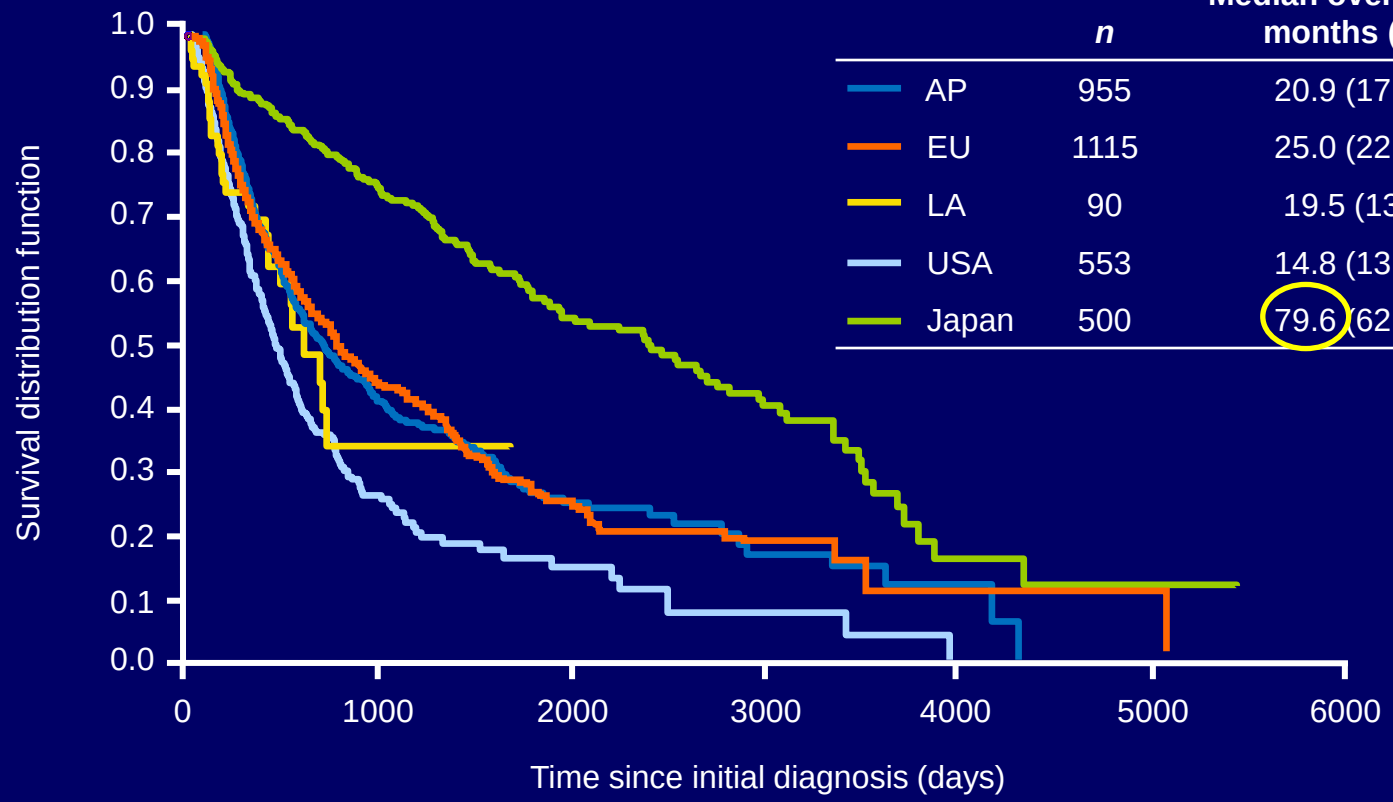
HCC Global Non-interventional Study: GIDEON



5 regions
39 countries
>3300 patients

Kudo M, et al. Liver Int 2016

Time from initial diagnosis to death by region



	n	Median overall survival, months (95% CI)
AP	955	20.9 (17.3-25.2)
EU	1115	25.0 (22.9-28.7)
LA	90	19.5 (13.5-NE)
USA	553	14.8 (13.1-17.0)
Japan	500	79.6 (62.1-96.0)

- Time from initial diagnosis to death was longest in Japan
- We also have to understand a caveat of lead-time bias

Kudo M, et al. Liver Int 2016

Time from initial diagnosis to death by BCLC stage at initial diagnosis

Median time from initial diagnosis to death, months (95% CI)	AP *n*=955	EU *n*=1115	LA *n*=90	USA *n*=553	Japan *n*=500	Overall *N*=3213[a]
BCLC stage A (*n*=686)	54.0 (10.3-NA)	49.3 (42.3-58.0)	23.3 (17.2-NA)	24.9 (18.4-53.5)	91.0 (76.6-113.1)	59.2 (51.9-67.5)
BCLC stage B (*n*=633)	31.0 (18.4-47.7)	27.3 (23.0-33.1)	22.2 (12.9-NA)	19.7 (11.1-36.8)	47.9 (40.9-86.2)	29.9 (25.6-39.0)
BCLC stage C (*n*=973)	10.3 (262-409)	11.0 (8.9-13.0)	11.2 (3.1-NA)	8.5 (6.2-10.2)	27.7 (16.6-40.8)	10.6 (9.4-12.4)
BCLC stage D (*n*=91)	8.9 (8.6-14.8)	11.0 (4.2-21.7)	NA	7.5 (4.5-12.8)	13.1 (NA-NA)	8.9 (6.2-13.1)
Overall	20.9 (17.3-25.2)	25.0 (22.9-28.7)	19.5 (13.5-NA)	14.8 (13.1-17.0)	79.6 (62.1-96.0)	25.5 (23.9-28.3)

- Time from initial diagnosis to death was longest in Japan, irrespective of BCLC stage

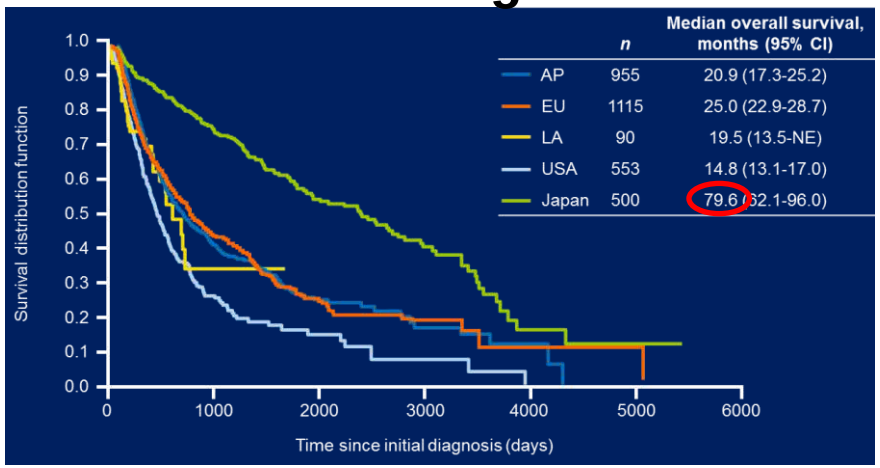
[a]Intention-to-treat population
NA, not available

Kudo M, et al. Liver Int 2016

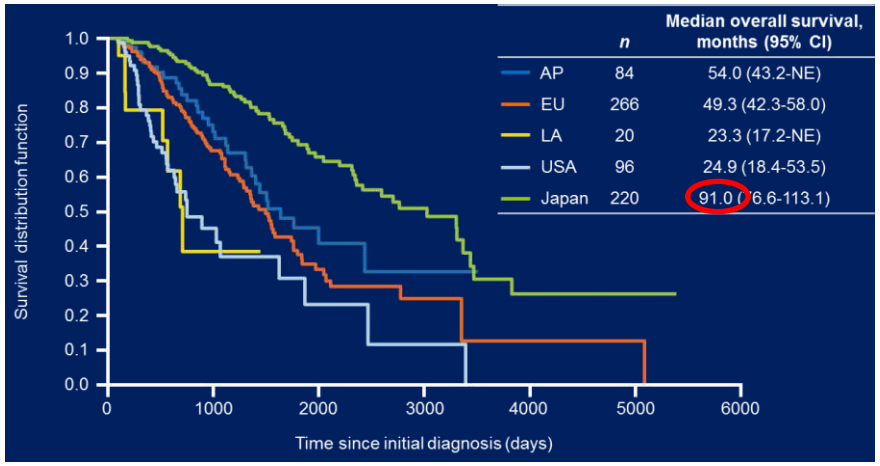
Global Non-Interventional Registry

Time from Initial Diagnosis to Death by BCLC stage

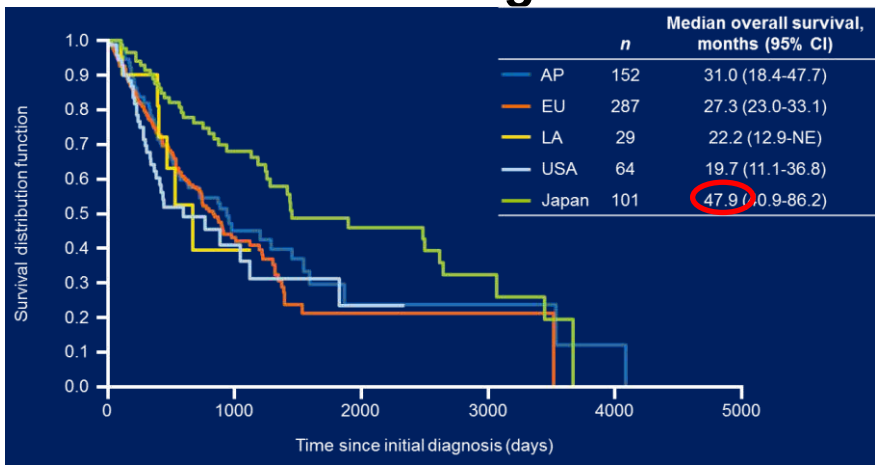
All stage



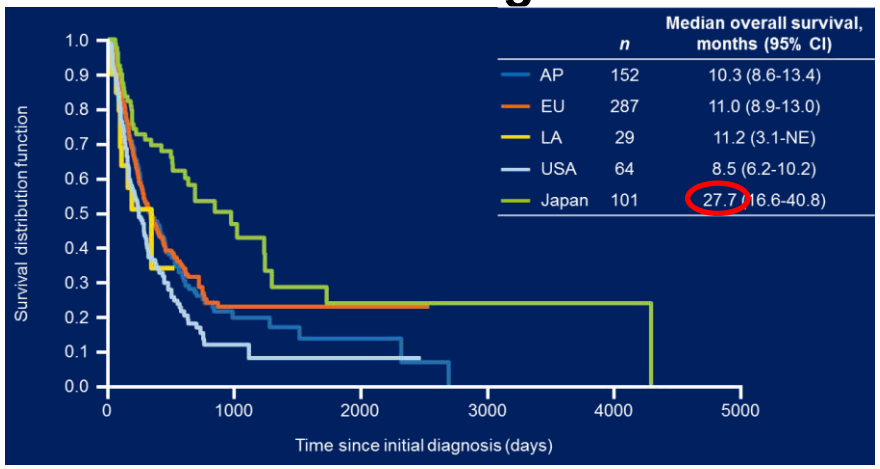
BCLC stage A



BCLC stage B



BCLC stage C

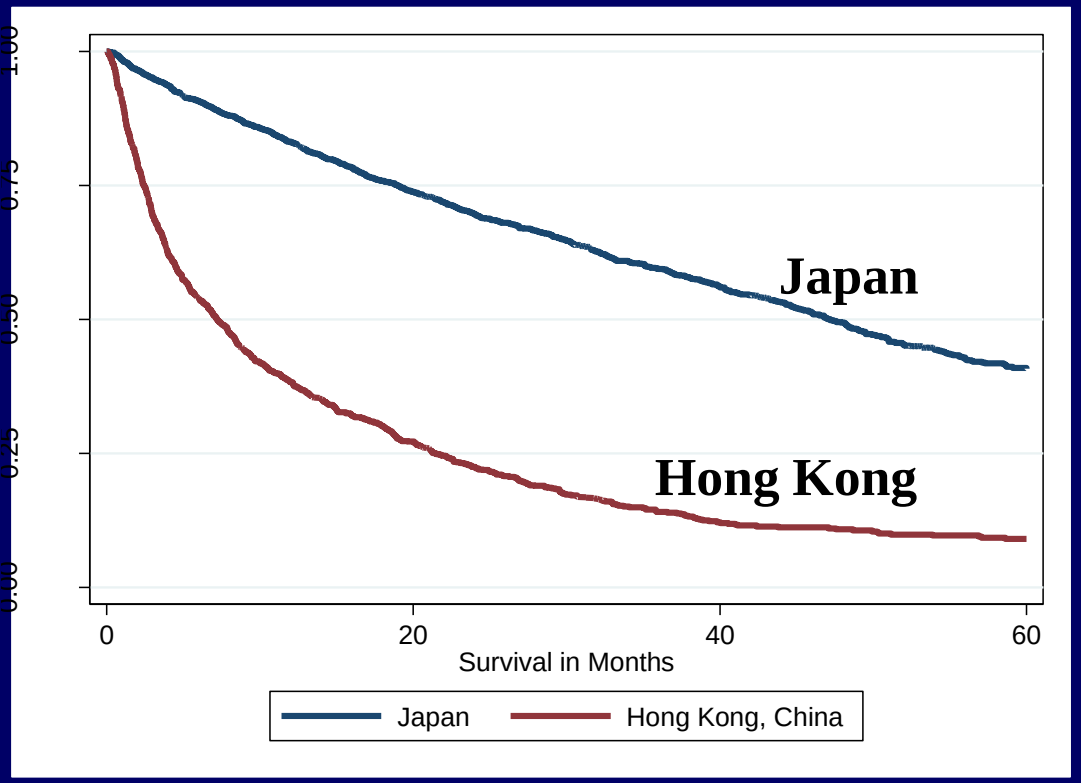


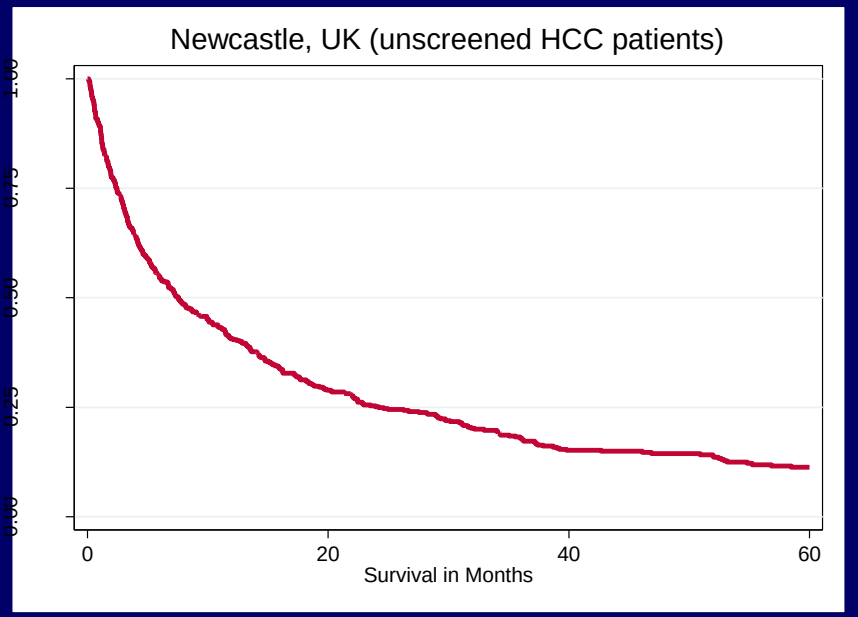
Kudo M et al. Liver Int. 2016;36(8):1196-205

Surveillance: Japan as a successful model

- Results of Nationwide Surveillance of HCC by JLCA
- Regional Difference of OS Results According to GIDEON, Non-interventional study
- Treatment Outcome in Japan and Hong Kong: Effect of Nationwide Surveillance

Overall Survival in Japan and Hong Kong





Country	N	Median (months)
Newcastle, UK	470	7.5(6-9.9)

Region	N	Median survival (months), (95% CI)	5year survival
Japan	2596	47.2 (44.6-49.5)	45-50%
Hong Kong, China	1108	7.2 (6.4-8.2)	10%

Johnson P et al, EASL 2014
Johnson P et al, Br J Cancer 2017

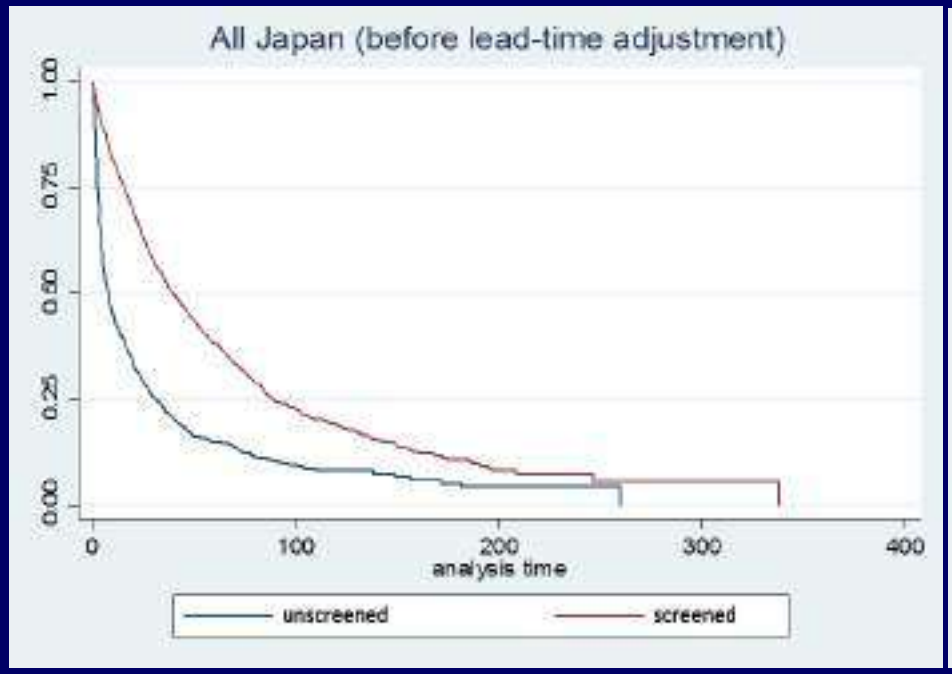
% Of Patients With Curative Treatments, Early Stage BCLC And Within Milan Criteria

Country	Curative Rx (%)	BCLC 0 and A (%)	Within Milan Criteria (%)
Japan	71.2 (n=2594)	65.7 (n=685)	58.9 (n=2473)
Hong Kong	15.7 (n=1112)	15.1 (n=517)	8.4 (n=1066)

1 year survival (%)		Japan	Hong Kong, China
HCV	BCLC early (0 and A)	92.6	83.3
HBV	BCLC early (0 and A)	94.8	89.9
2 year survival (%)		**Japan**	**Hong Kong, China**
HCV	BCLC early (0 and A)	81.9	75.0
HBV	BCLC early (0 and A)	74.2	76.9

Johnson P et al, EASL 2014
Johnson P et al, Br J Cancer 2017

Impact of Screening - Allowing For Lead Time Bias*



	Subjects N=	**Median in months(CI)**
Unscreened	794	**7.5 (6-9)**
Screened	1689	**39.4 (36-43)**

	Subjects N=	**Median in months(CI)**
Unscreened	794	**7.5 (6-9)**
Screened	1689	**22.3(21-25)**

*Method reference: Duffy SW, et al., Correcting for lead time bias in estimating the effect of screen detection on cancer survival. Am J Epidemiol. 2008

Johnson P et al, EASL 2014
Johnson P et al, Br J Cancer 2017

Summary and Conclusion

Circumstantial evidence supports surveillance seems to increase likelihood of curative therapy and prolonged survival

Important issue

- Nationwide surveillance *DID* decrease the disease specific mortality in Japan
- Surveillance is easier/done better in Japan
- Treatment is just better in Japan

Johnson P et al, EASL 2014
Johnson P et al, Br J Cancer 2017

Outcome in Japanese patients with HCC seems to be the best in the world *in terms of nationwide survival rate* mainly due to early detection of HCC through established nation-wide surveillance program.

Johnson P et al, EASL 2014
Johnson P et al, Br J Cancer 2017

Outline

- Overview of HCC trend in Japan
- Overview of HCC outcome in Japan
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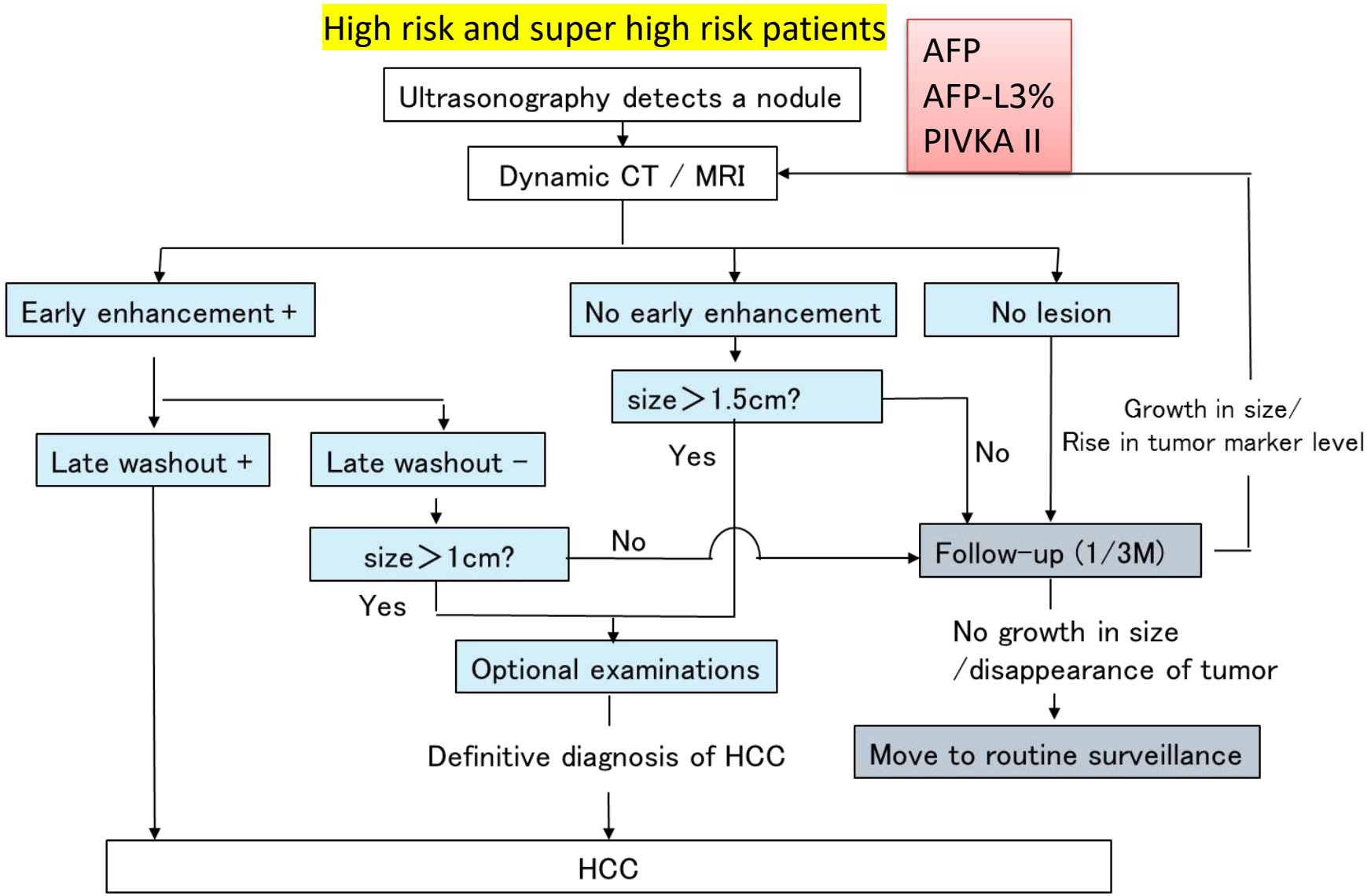
- Innovative treatment strategy in Advanced stage HCC
- Role of Multidisciplinary Team
- Lessons learned from Japan’s experience
- Future innovations and Personalized Medicine

JSH clinical practice guideline for surveillance and diagnosis of HCC



JSH HCC Clinical Practice Guideline 2005, 2009, 2013, 2017, 2021

Typical Nationwide Surveillance Methods: Definition of High-risk Group

High-risk
- Chronic hepatitis B
- Chronic hepatitis C
- Liver cirrhosis

Very-high-risk
- Hepatitis B cirrhosis
- Hepatitis C cirrhosis

In practice, non-cirrhotic NASH/NAFLD patients are under surveillance

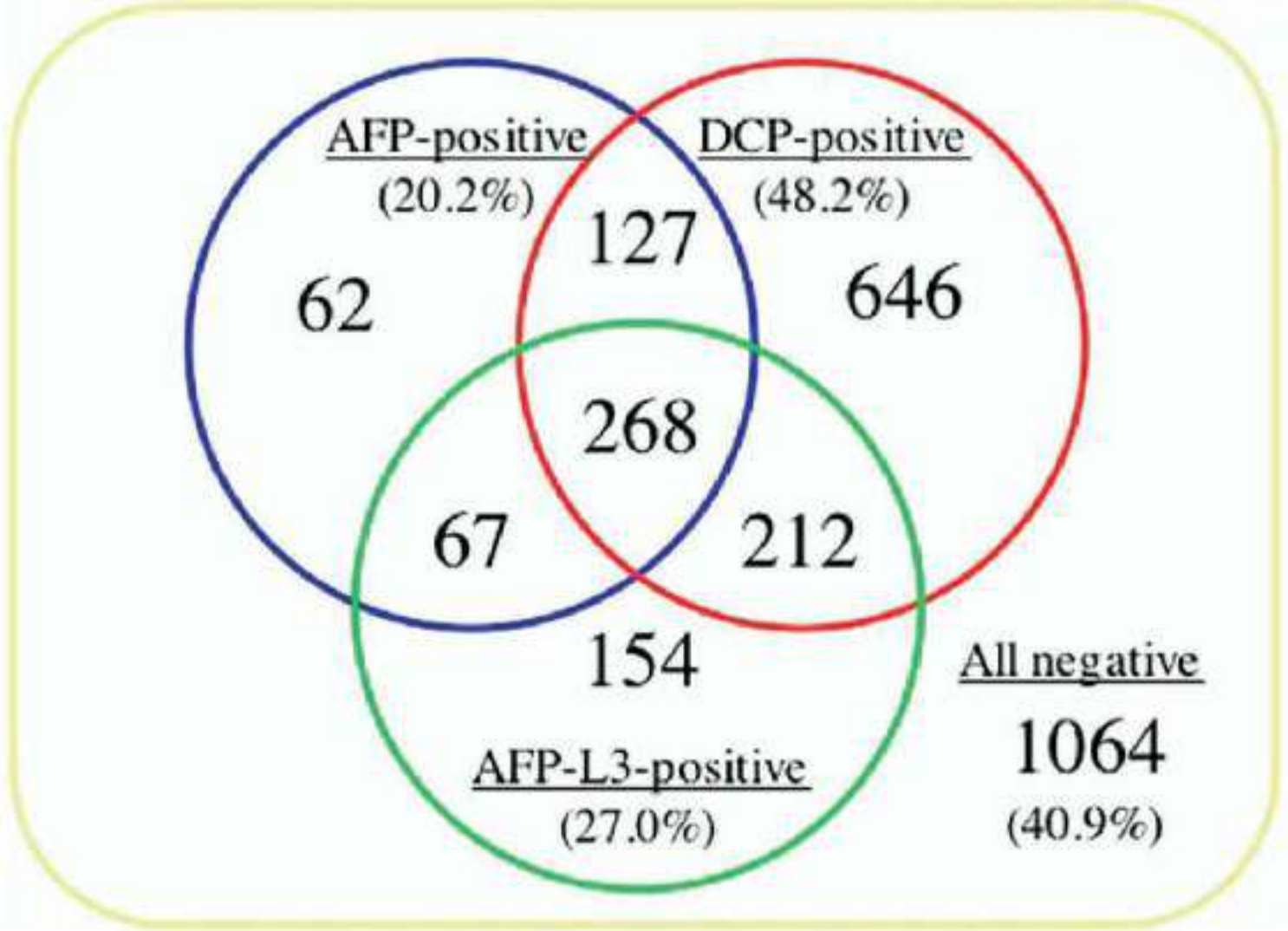
JSH HCC Clinical Practice Guideline 2005, 2009, 2013, 2017, 2021

Tumor Markers for HCC in Japan

- AFP
- AFP-L3
  - Lectin-binding fraction of AFP
- PIVKA-II (DCP)
  - Prothrombin induced by Vit. K absence (des-γ -carboxy-prothrombin)

All are covered by social health insurance in Japan.

JSH HCC Clinical Practice Guideline 2005, 2009, 2013, 2017, 2021



Since there is no correlation between these 3 tumor markers, AFP, DCP (PIVKA-II), and AFP-L3 play a complementary role.

Toyoda H, et al Clinical Gastroenterol Hepatol 2006

Clinical practice guideline

Recommendation

For the surveillance of small hepatocellular carcinoma, measurement of two or more tumor markers is recommended. (grade A)

JSH HCC Clinical Practice Guideline 2005, 2009, 2013, 2017, 2021

Follow up methods for high risk patients in all over Japan

- High Risk patients
  - US at intervals of 6mo.
  - AFP/PIVKA-II/AFP-L3 every 6mo.

- Very High Risk patients
  - US every 3-4 mo.
  - AFP/PIVKA-II/AFP-L3 every 3-4 mo.
  - Option: dynamic CT/MRI every 6-12 mo.

These HCC surveillance program has been well implemented throughout Japan since education to patients and private practitioner were established since 1980s.

JSH HCC Clinical Practice Guideline 2005, 2009, 2013, 2017, 2021

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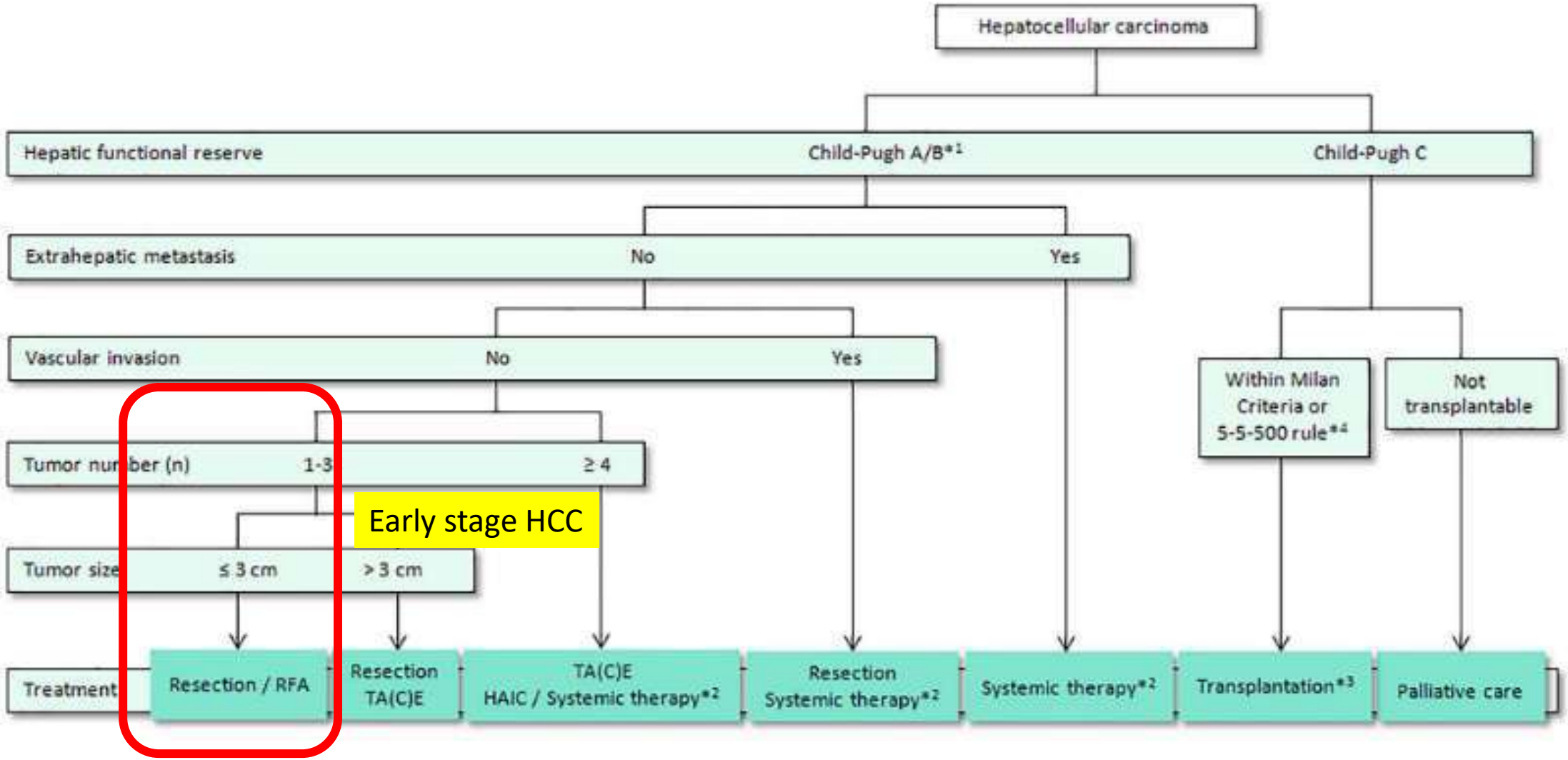
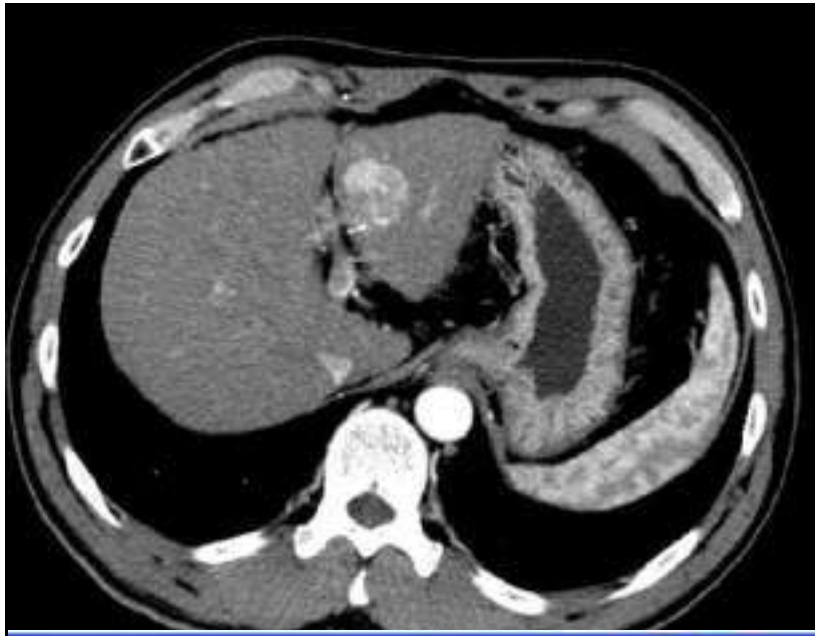
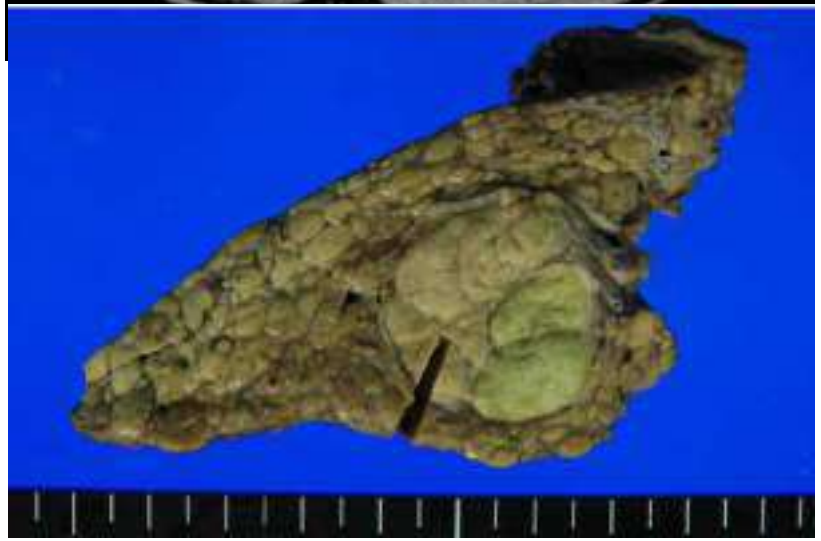
JSH HCC Guidelines 2021 Algorithm for Treatment



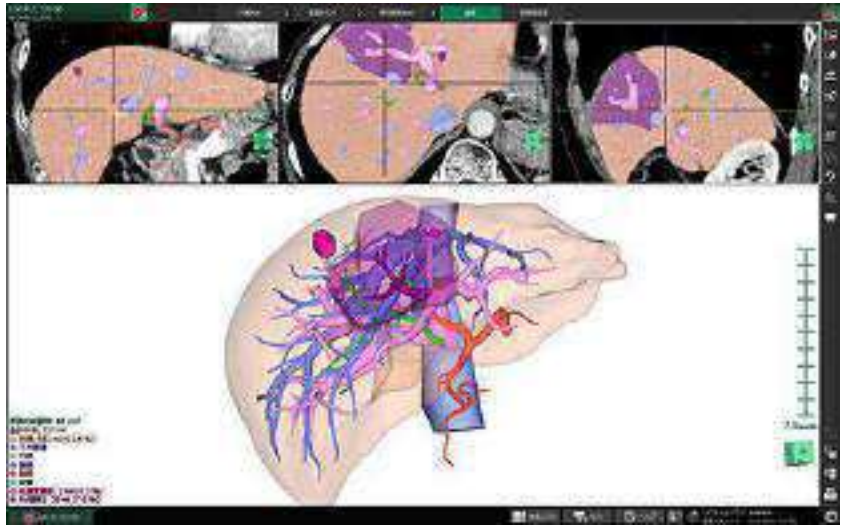
Hasegawa K, Tateishi R, Kudo M, et al. Hepatol Res. 2023

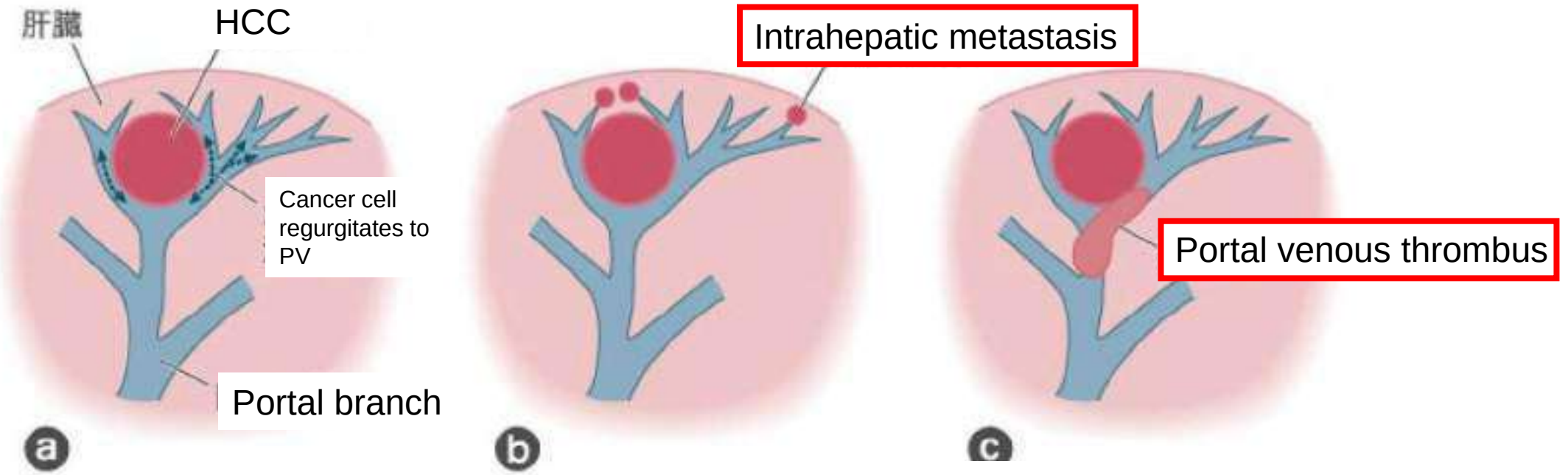
Resection





- Child-Pugh grade A
- Solitary tumor
- Laparoscopic and robotic surgery are reimbursed and frequently performed.



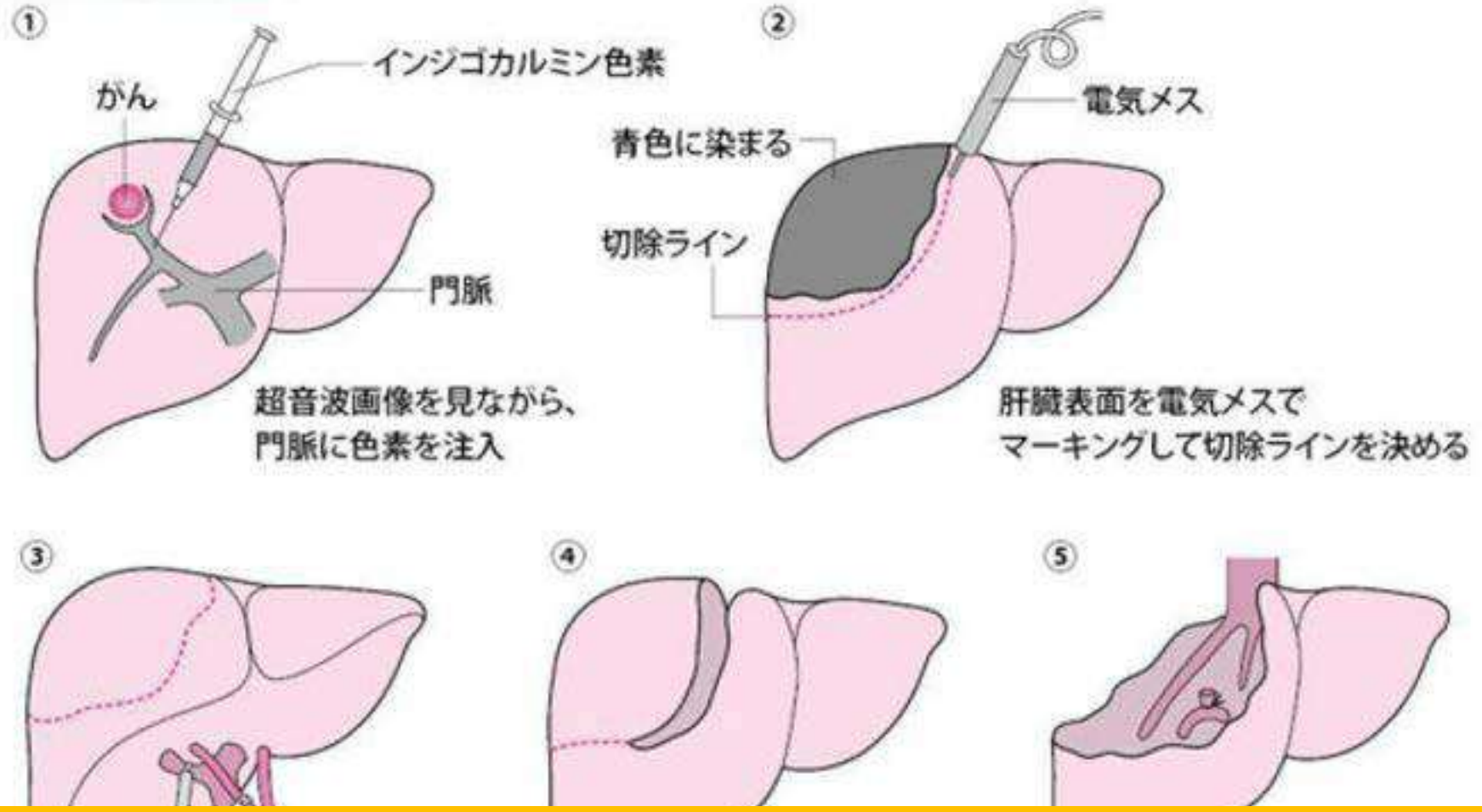


Subsegmental anatomical resection was invented in Japan by Prof. Makuuchi in 1980s, and spread to allover the world.

Anatomical resection

Radiofrequency ablation

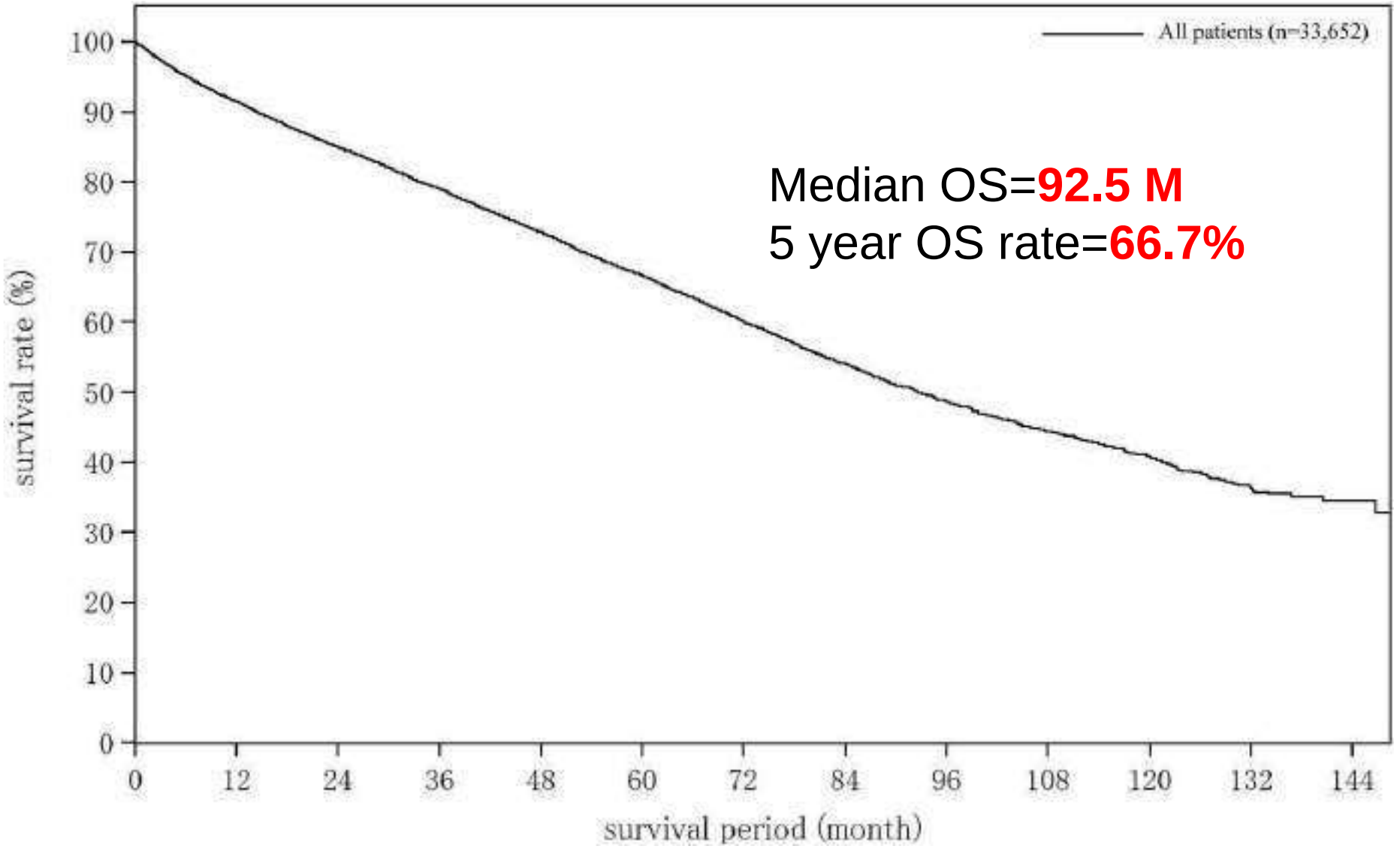
Special technique (ICG injection into the portal branch) for anatomical resection



This technique remove enough tumor, preventing recurrence, while preserving liver function

Makuuchi M, et al：Surg Gynecol Obstet 161：346-350, 1985より改変

Overall Survival by Surgical Resection (n=33,652)

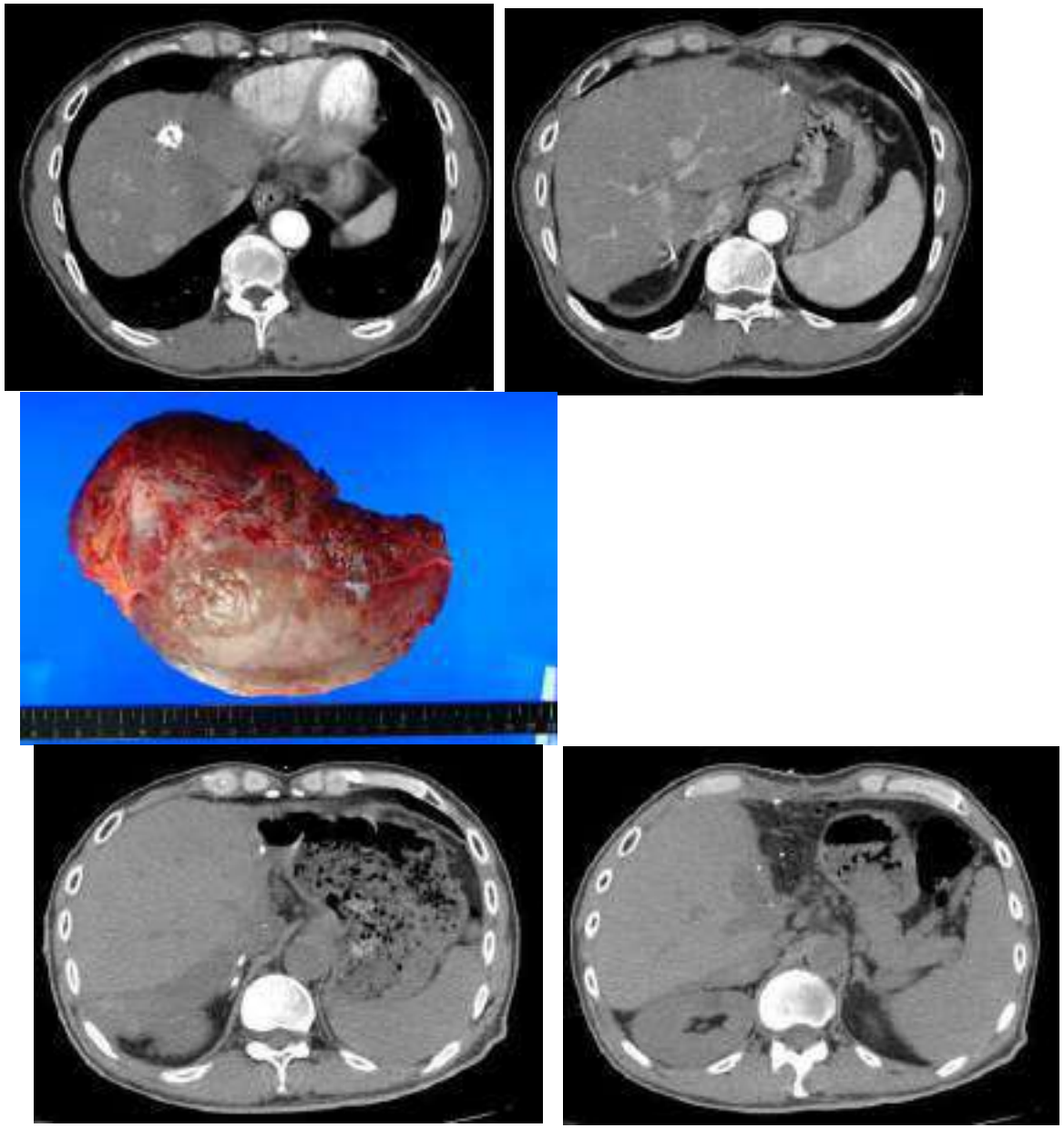


Median OS=**92.5 M**

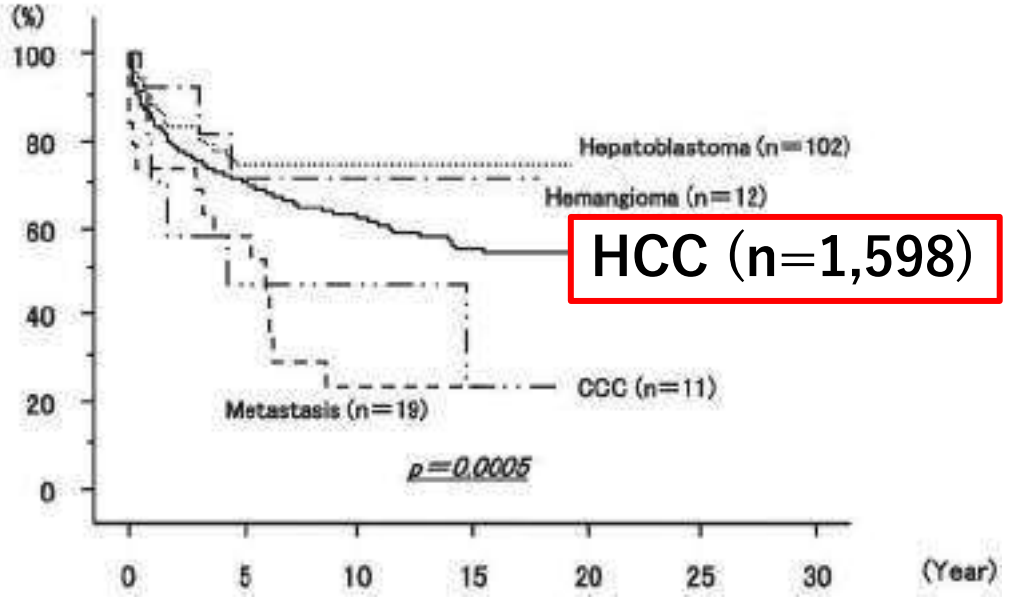
5 year OS rate=**66.7%**

Kudo M, et al. 22nd Nation-wide follow-up survey by JLCA. Hepatol Res. 2022

Liver Transplantation

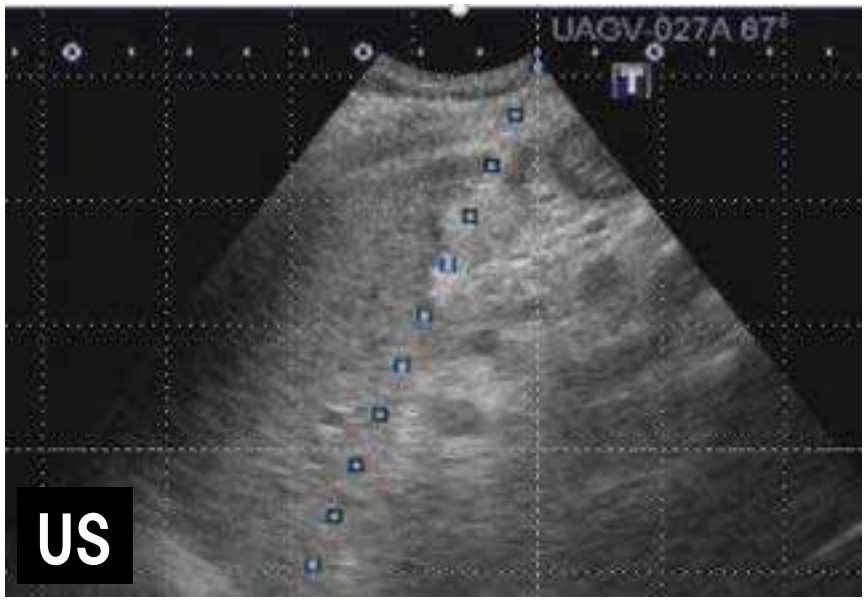


20 y survival rate: 60%

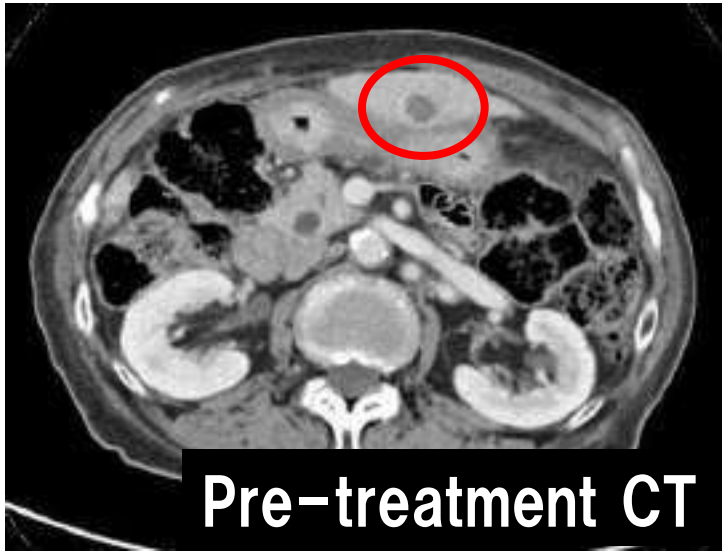


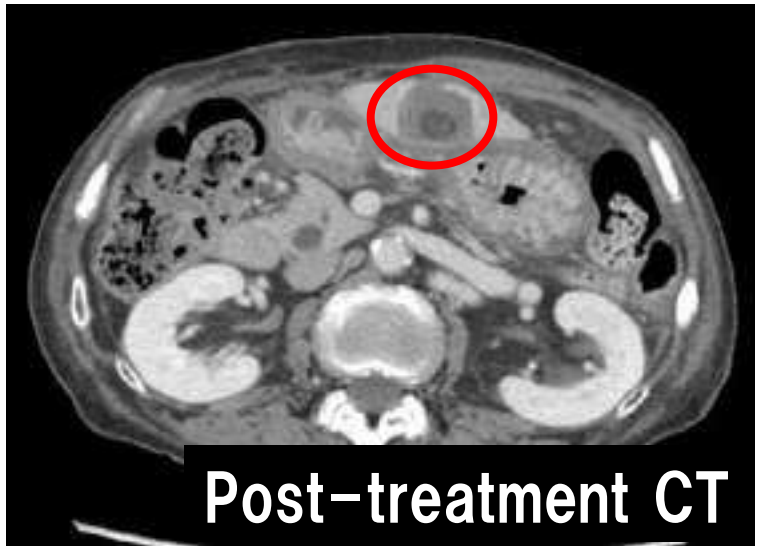
Japan Transplant Society；2017

Ablation（Radiofrequency ablation，RFA）

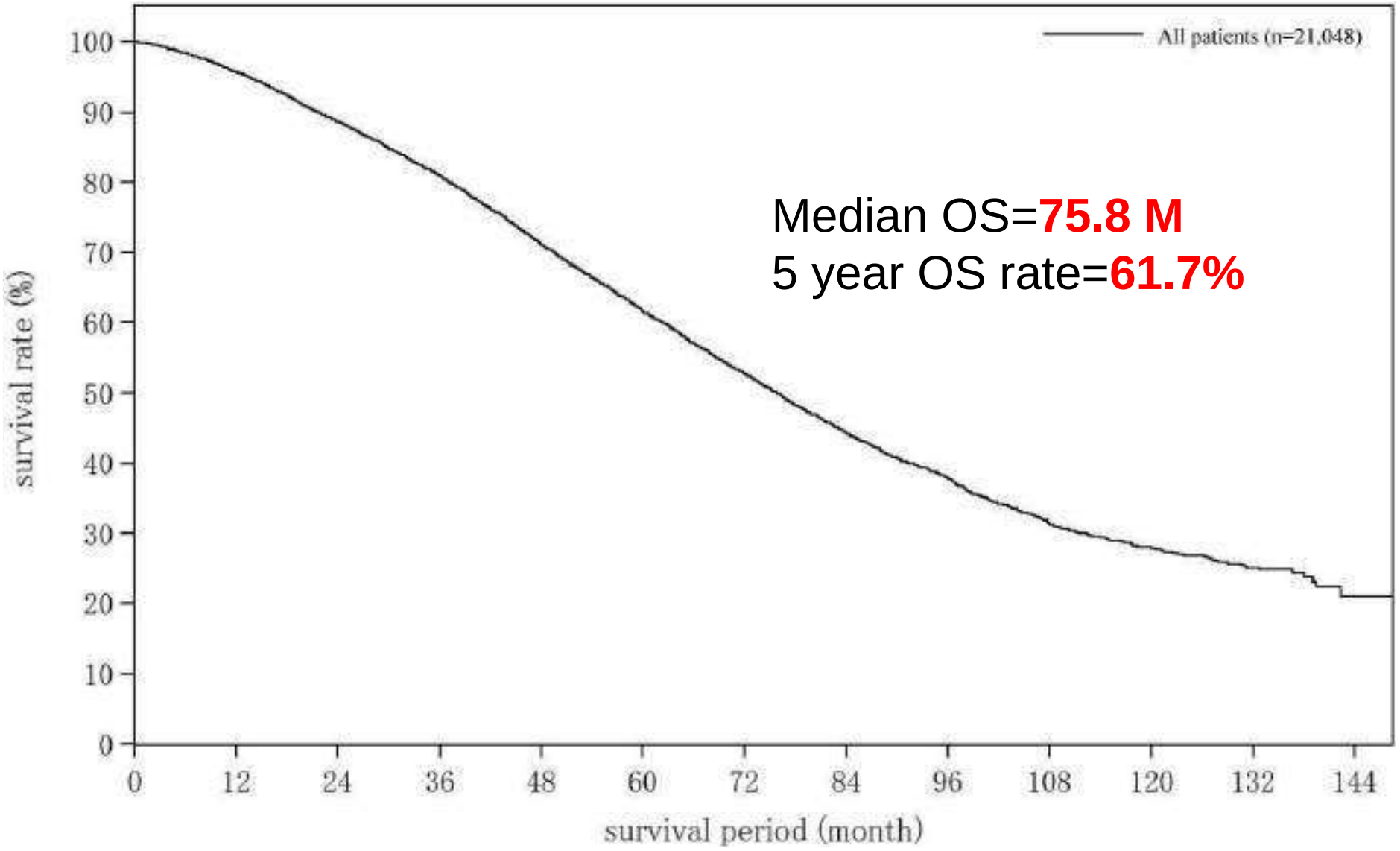


Ablation with enough safety margin





Overall Survival by Radiofrequency Ablation (RFA)(n=21,048)



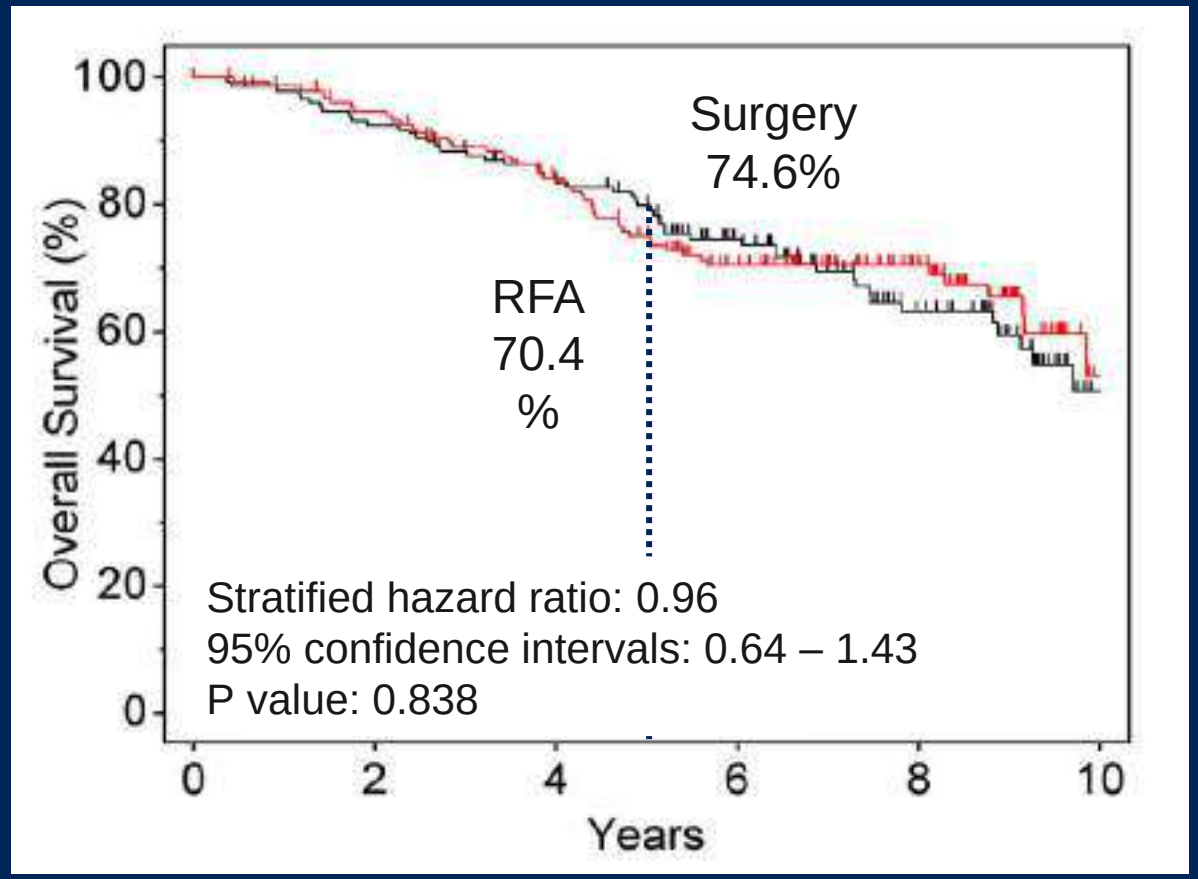
Median OS=**75.8 M**

5 year OS rate=**61.7%**

Kudo M, et al. 22nd Nation-wide follow-up survey by JLCA. Hepatol Res. 2022

SURF Trial: Prospective multicenter P3 trial

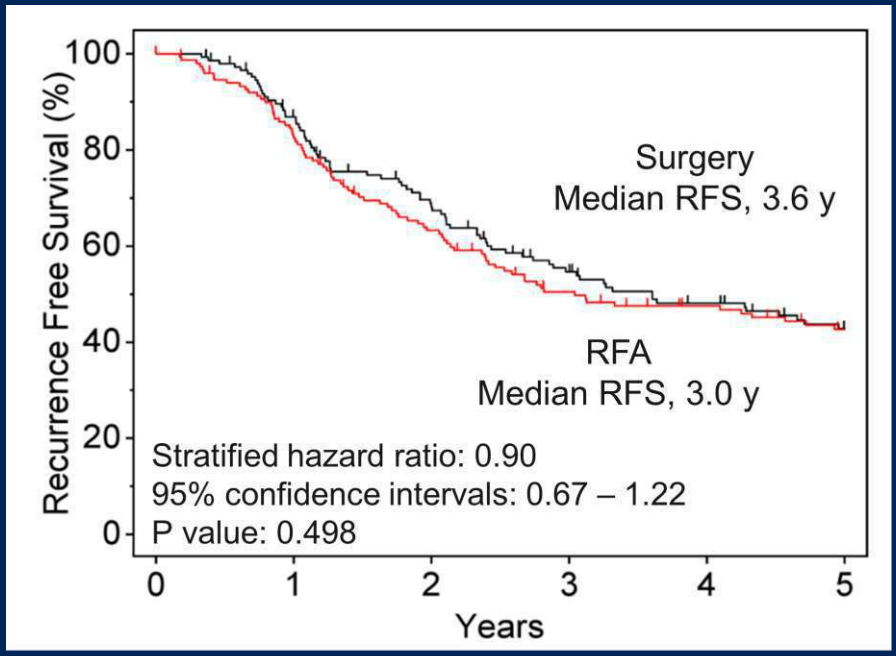
OS, Surgery vs. RFA



Number at risk

150	136	118	82	45	9
152	139	119	84	53	5

RFS Analysis Updates



Number at risk

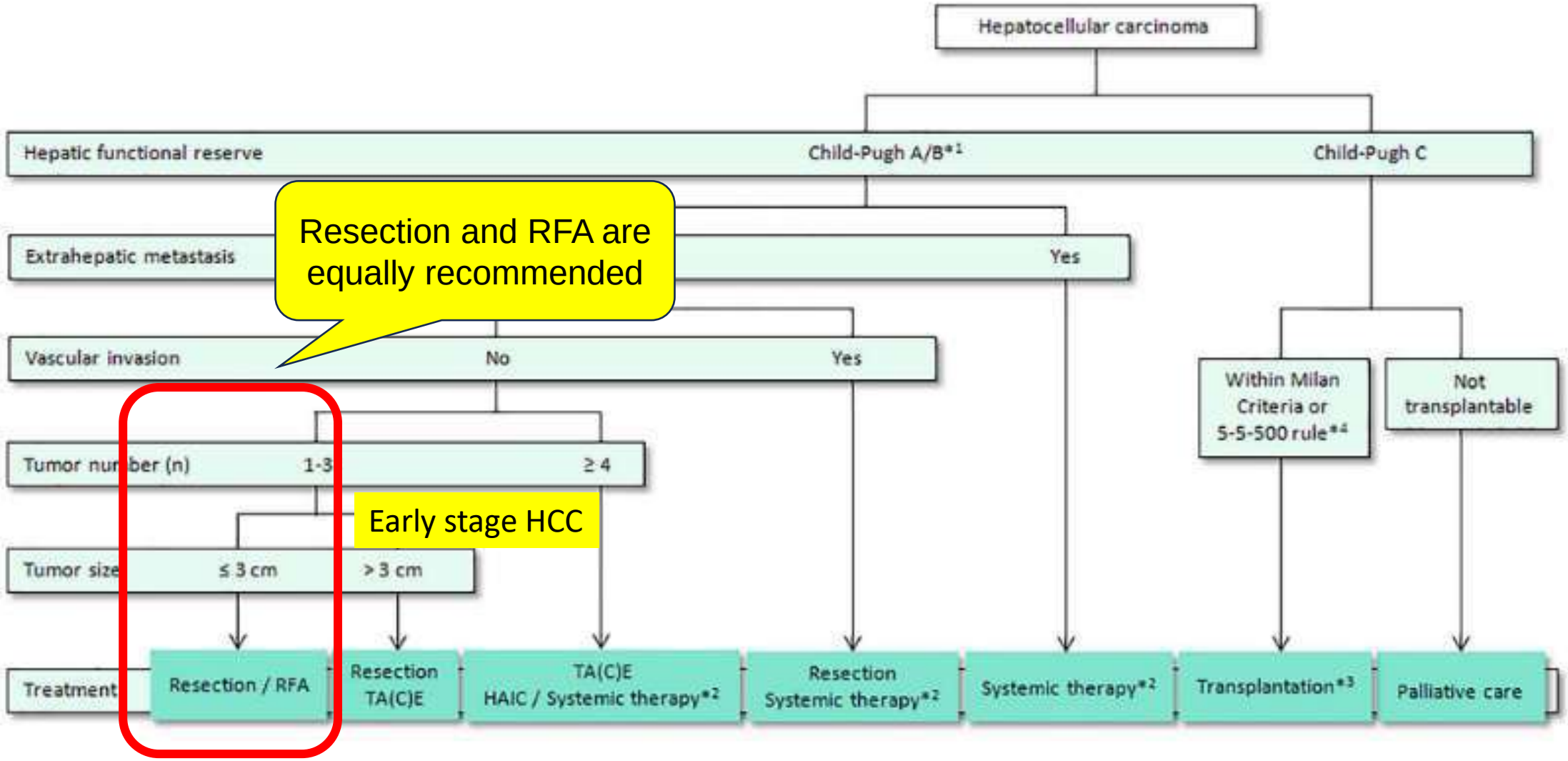
150	123	93	70	58	47
152	122	91	69	60	50

Median follow-up time

Surgery: 6.4 years

RFA: 6.6 years

JSH HCC Guidelines 2021 Algorithm for Treatment



Hasegawa K, Tateishi R, Kudo M, et al. Hepatol Res. 2023

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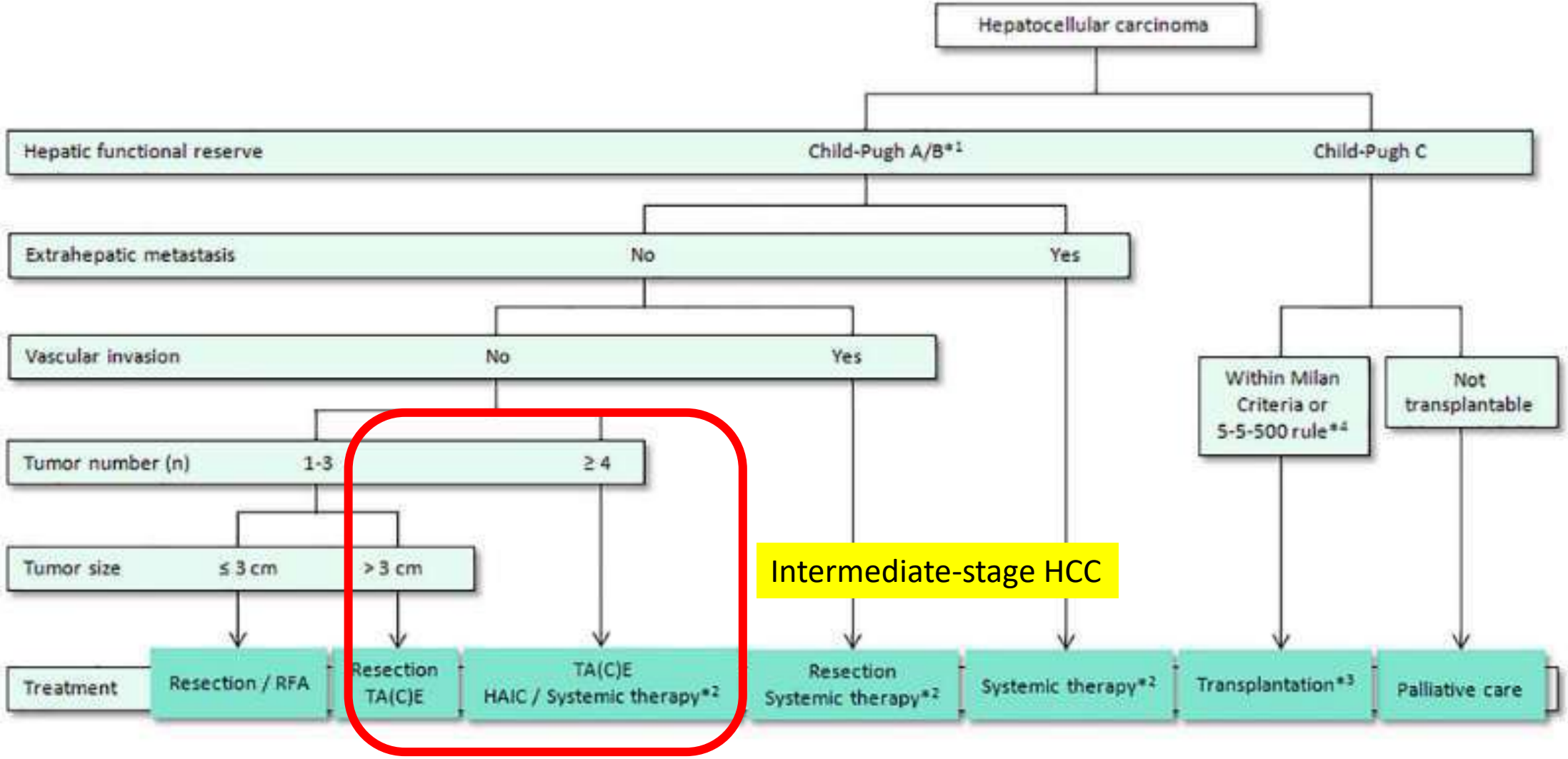


Hasegawa K, Tateishi R, Kudo M, et al. Hepatol Res. 2023

Ryusaku Yamada, M.D.
Morio Sato, M.D.
Mamoru Kawabata, M.D.
Haruki Nakatsuka, M.D.
Kenji Nakamura, M.D.
Sumio Takashima, M.D.

Hepatic Artery Embolization in 120 Patients with Unresectable Hepatoma[1]

Invention of TACE: first in the world in Japan in 1983 by Prof. Yamada

Transcatheter hepatic artery embolization was performed in 120 patients with unresectable hepatoma. The cumulative one-year survival rate was 44%. In most cases follow-up angiography revealed the selective disappearance of tumor vessels, and computed tomography demonstrated a marked decrease in tumor density without any changes in the surrounding liver parenchyma. Histologic examination in 14 cases confirmed these findings.

Index terms: Arteries, therapeutic blockade, 9.129 • (Hepatic artery, therapeutic embolization, 9[52].129) • (Liver, malignant hepatoma, 7[61].329) • Liver neoplasms, blood supply • Liver neoplasms, therapy

Radiology 148: 397–401, August 1983

HEPATOMA is a relatively common malignant tumor in Japan, and patients with this neoplasm have a poor prognosis. The first choice of treatment is hepatectomy, but most cases are considered inoperable due to extreme tumor extension at the time of diagnosis and accompanying advanced cirrhosis. According to the 1979 report of the Liver Cancer Study Group of Japan (1), only 9% of hepatoma patients underwent hepatectomy. The report also concluded that the one-year survival rate after surgery was only 28%. Chemotherapy produced even worse results: the survival rate one year after treatment was 7%, and the mean length of survival was 3 to 6 months.

Since 1977 we have performed transcatheter arterial embolization in 120 cases of unresectable hepatoma. This report describes our experience with embolization, which demonstrates far more satisfactory results than other existing treatments.

MATERIALS AND METHODS

Two hundred thirty-five embolization procedures were performed in 120 patients with unresectable hepatoma from June 1977 to May 1982. Repeat embolizations (2 to 7 procedures) were performed in 45%

Yamada R, et al. Radiology 1983

Changing Treatment Strategy of Intermediate Stage-HCC

TACE

- Matsui O(1993) Subseg Lip-TACE
- Ohishi H(1985) Lip-TACE
- Uchida H(1990) Seg Lip-TACE
- Llovet JM(2003) TACE vs BSC Meta-analysis
- Yamada R(1983) GS-TAE
- Miyayama S(2007) Ultraselective TACE
- PRESIDENT(2016) DEB-TACE vs cTACE

Concept of TACE Failure：
Kudo M, et al. JSH Guideline（2017）

Concept of TACE Suitable：
Kudo M, et al. JSH Consensus(2020)
Kudo M. APPLE Consensus（2020）

1983～ | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023

TACE+Systemic therapy

Because of the rapid advances of systemic therapy, TACE＋Systemic therapy has been becoming a SOC

Japan P2
TACTICS(2018)
SOR + TACE vs TACE

Multicenter POC
ABC Conversion(2023)
Atezo/Bev + Op, RFA, TACE

Japan P2
TACTICS-L(2022)
LEN -TACE

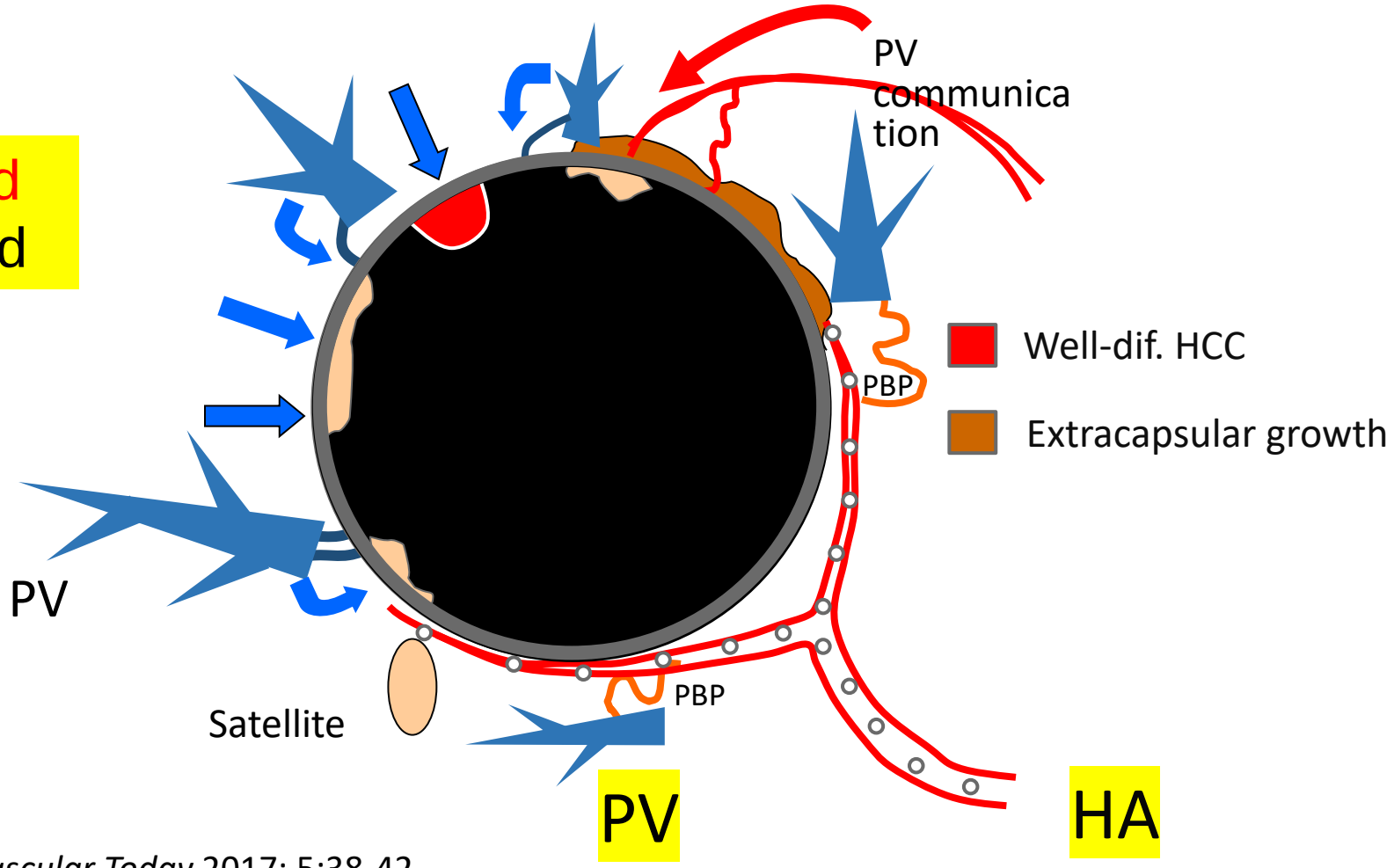
Global P3
EMERALD-1(2024)
Durva±Bev TACE vs TACE

China P3
LAUNCH(2022)
LEN-TACE vs LEN
BCLC-B+C

Global P3
LEAP-012 (2024)
LEN + PEM +TACE vs TACE

Non-selective TACE

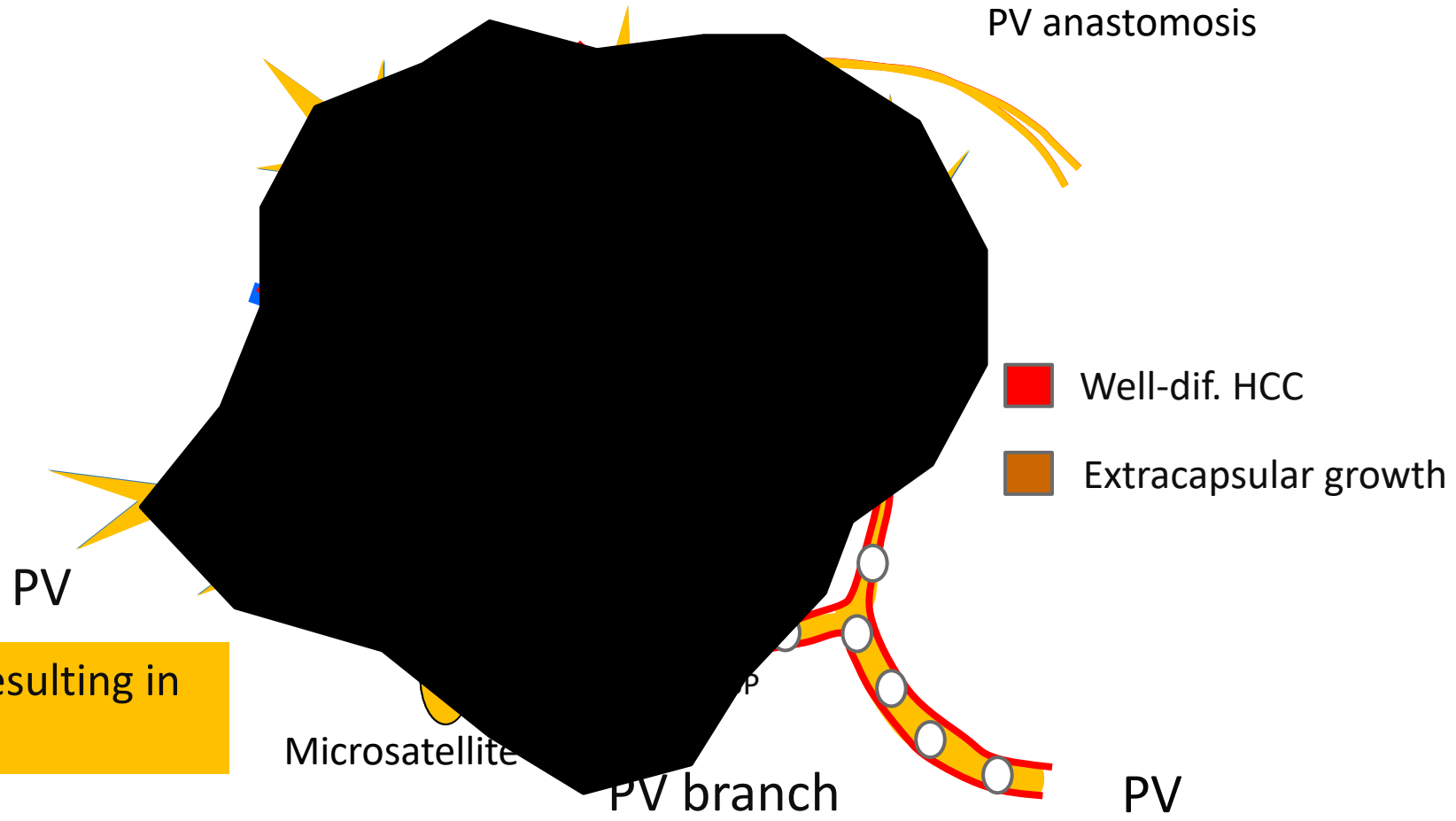
Inflow of portal blood when HA is occluded



Miyayama S and Matsui O. *Endovascular Today* 2017; 5:38-42.

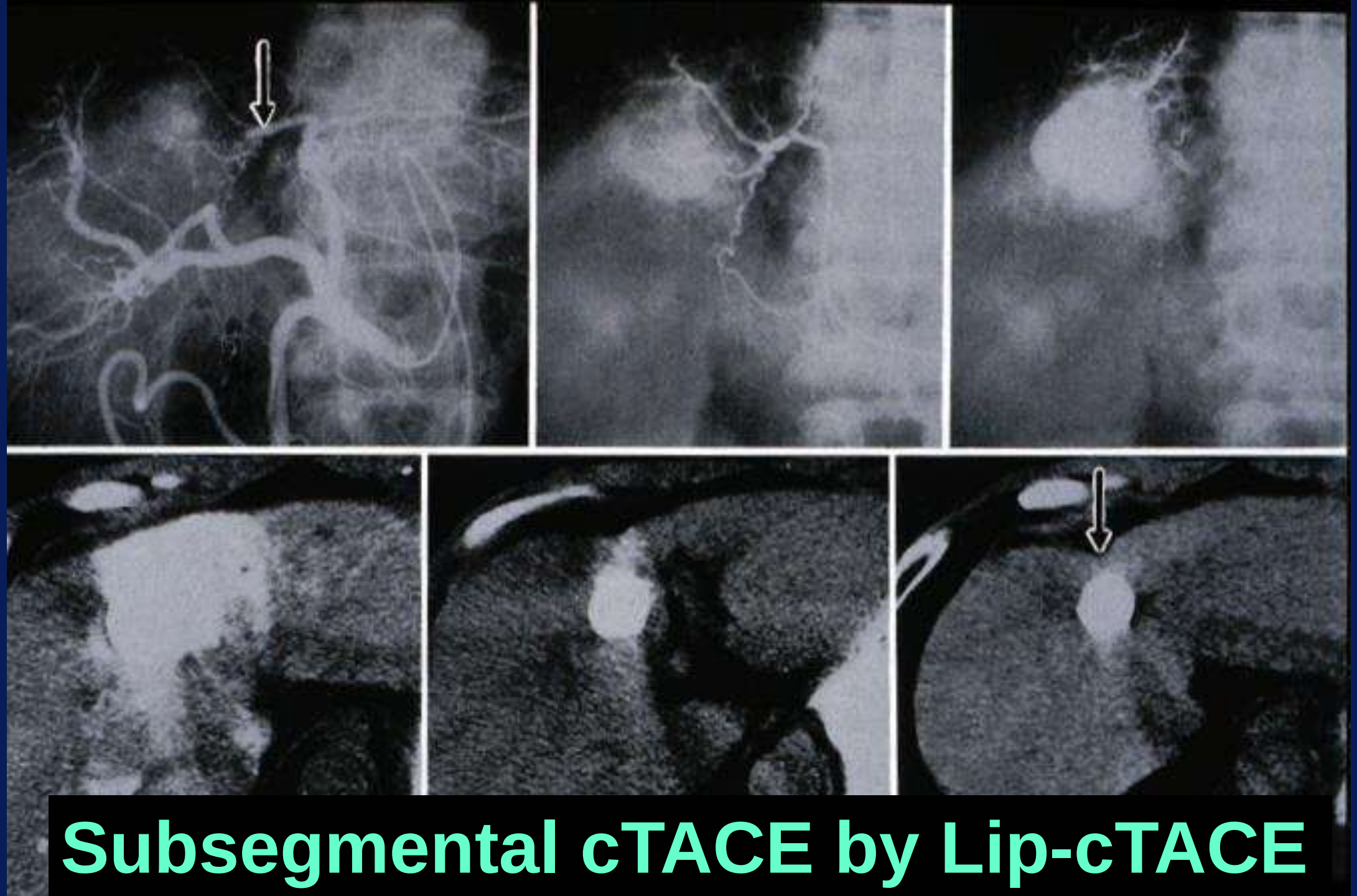
Superselective cTACE

Intraarterial Lipiodol regurgitate to the PV, via PBP or drainage vessel



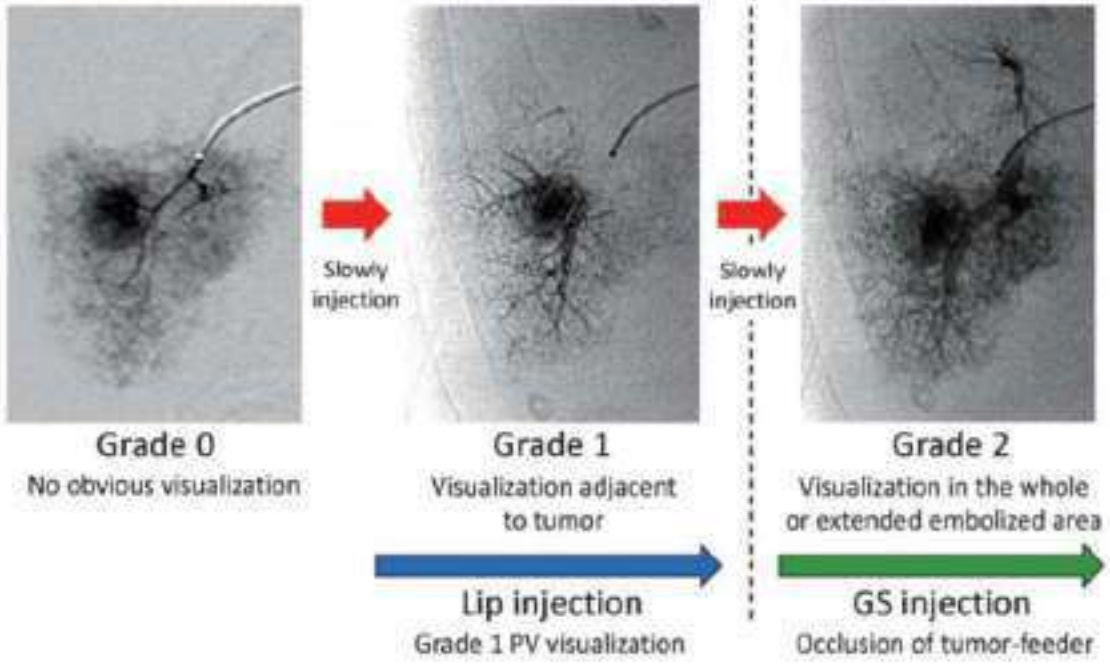
Lipiodol blocks PV flow, resulting in Complete necrosis

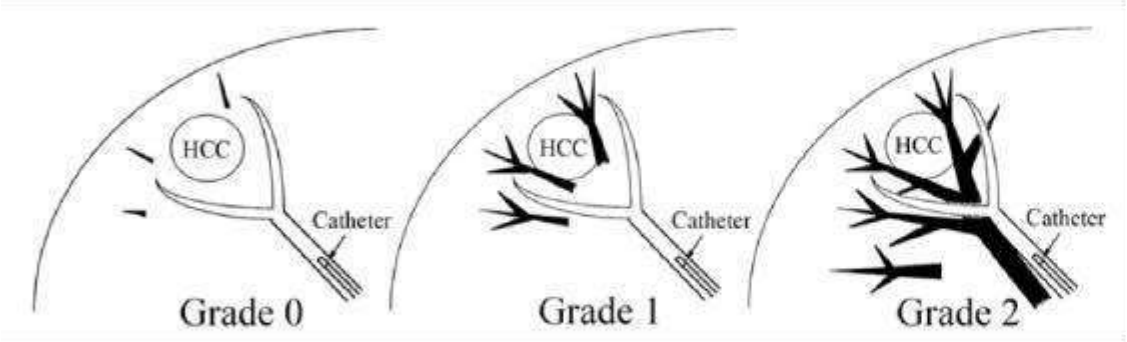
Miyayama S and Matsui O. *Endovascular Today* 2017; 5:38-42.

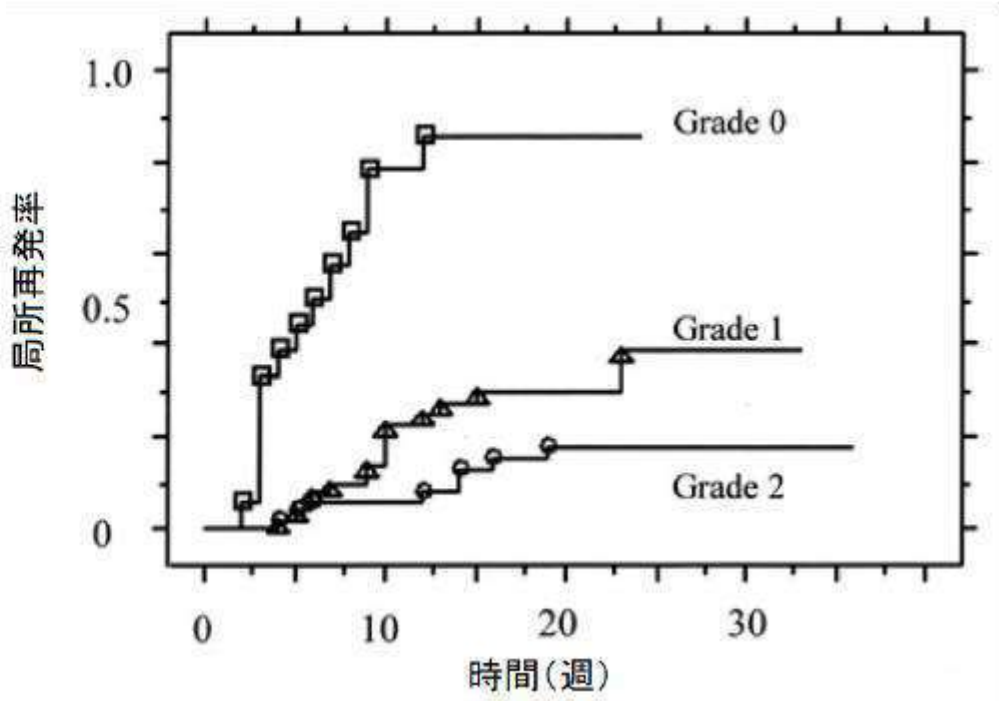


Subsegmental cTACE by Lip-cTACE

Grade of regurgitation of Lipiodol in the portal vein correlates to the local control rate.

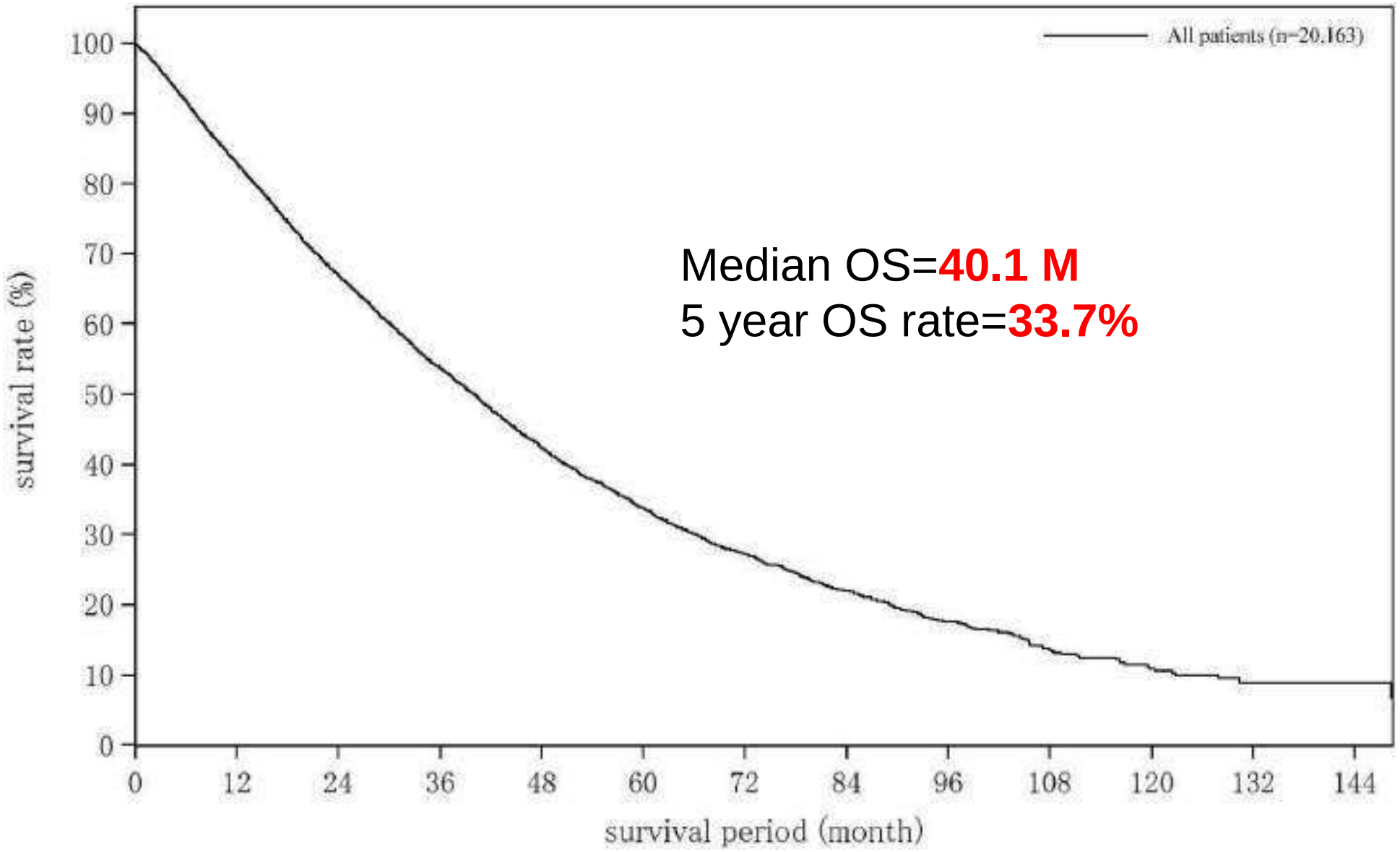






Miyayama S, Matsui O. 2016;27:1269–1278.
Miyayama S, et al. JVIR 2007;18:365-376

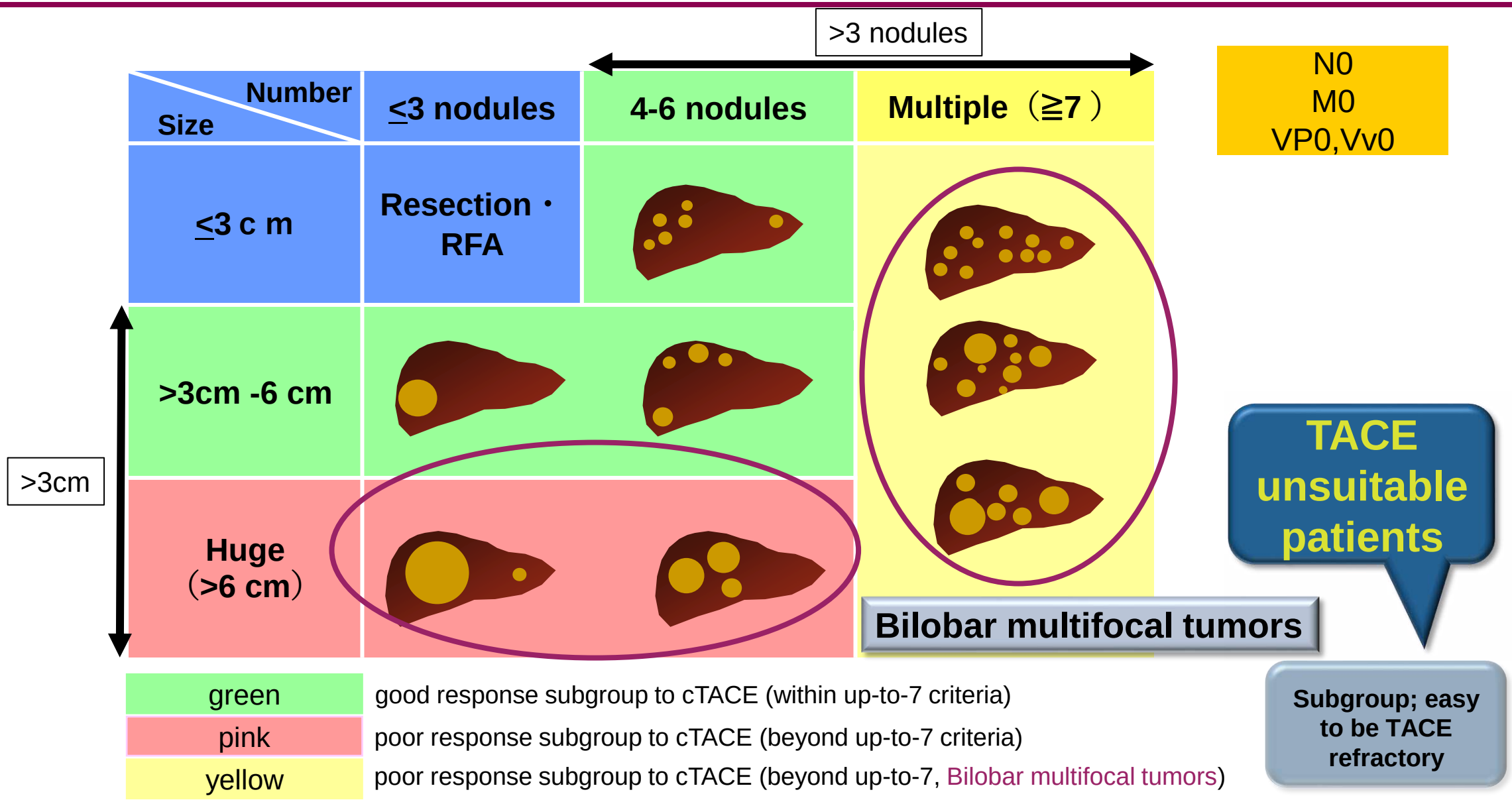
Overall Survival by TACE (n=20,163)



Median OS=**40.1 M**
5 year OS rate=**33.7%**

Kudo M, et al. 22nd Nation-wide follow-up survey by JLCA. Hepatol Res. 2022

Heterogeneity and treatment strategy of intermediate stage HCC (Kinki Criteria)



APPLE Consensus Statements

APPLE Consensus Members

Masatoshi Kudo
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Liver Cancer

Consensus Statement

A Changing Paradigm for the Treatment of Intermediate-Stage Hepatocellular Carcinoma: Asia-Pacific Primary Liver Cancer Expert Consensus Statements

Masatoshi Kudo[a] Kwang-Hyub Han[b] Sheng-Long Ye[c] Jian Zhou[d] Yi-Hsiang Huang[e,f] Shi-Ming Lin[g,h] Chung-Kwe Wang[i] Masafumi Ikeda[j] Stephen Lam Chan[k] Su Pin Choo[l] Shiro Miyayama[m] Ann Lii Cheng[n–p] on behalf of the APPLE Association

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Kudo M et al, Liver Cancer 2020

Criteria for TACE unsuitability

APPLE Consensus Statement

CQ. 9 ：What is TACE-unsuitable?

(i) Unlikely to respond to TACE:
Confluent multinodular type, massive or infiltrative type, simple nodular type with extranodular growth, poorly differentiated type, intrahepatic multiple disseminated nodules, or sarcomatous changes after TACE

(ii) Likely to develop TACE failure/refractoriness:
up-to-7 criteria out nodules

(iii) Likely to become Child-Pugh B or C after TACE:
up-to-7 criteria out nodules (especially, bilobar multifocal HCC),
mALBI grade 2b

JSH Consensus Staement

Table 6-22：TACE-unsuitable patient population

①Likely to develop TACE failure/refractoriness
- up-to-7 criteria out nodules

②Likely to become Child-Pugh B after TACE
- up-to-7 criteria out nodules
（especially , bilobar multifocal HCC）
- ALBI grade 2（especially mALBI grade2B）

③Unlikely to respond to TACE
- Confluent multinodular type, massive or infiltrative type
- simple nodular type with extranodular growth
- poorly differentiated type
- intrahepatic multiple disseminated nodules
- sarcomatous changes after TACE

Kudo M et al :Treatment of Intermediate-Stage HCC: APPLE Consensus Statement. Liver Cancer 2020
Kudo M, et al. JSH Consensus Liver Cancer 2021. Kudo M, et al. JSH: Clinical practice manuals for hepatocellular carcinoma 4th edition, 2020.

TACTICS-L Study Schema

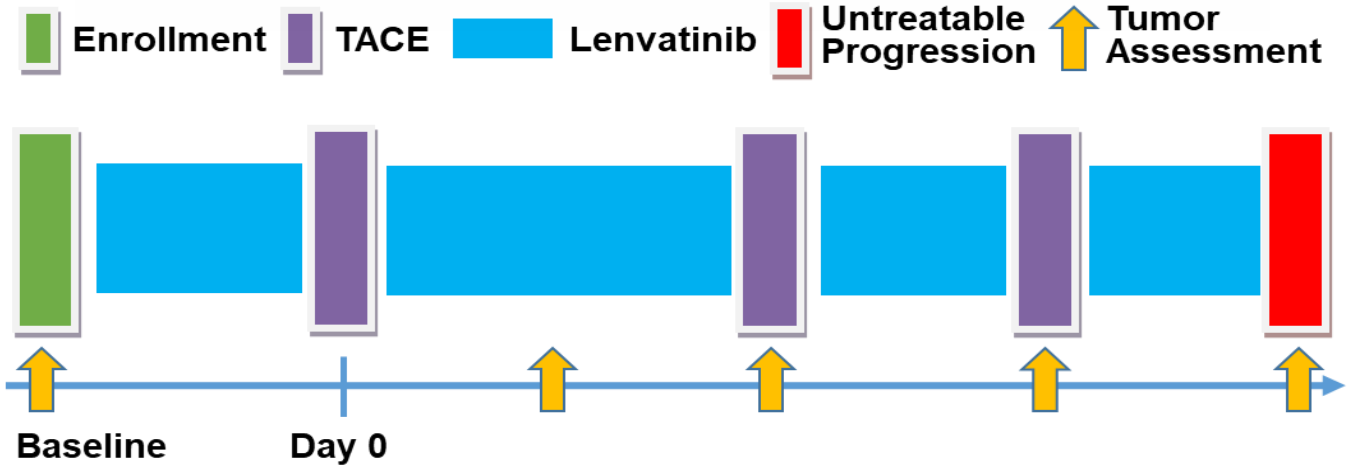
- A Phase II, prospective, multicenter, single-arm study was conducted at 21 Japanese institutions between February 2019 and April 2021.
- Efficacy assessments were performed on the ITT population (All eligible subjects). Safety assessments were performed on subjects who received at least one dose of lenvatinib or TACE procedure

Study Schema

<Inclusion criteria>
- Unresectable HCC
- Child-Pugh ≤6
- Prior TACE 0-2
- Tumor size ≤10cm
- Tumor Number ≤10
- ECOG-PS: 0 or 1

<Exclusion criteria>
- Vascular invasion
- Extrahepatic spread

LEN+TACE Combination



<Primary Endpoint>
- Progression Free Survival (PFS) by RECICL

<Secondary Endpoints>
- TTUP (Time to untreatable progression)
- PFS by mRECIST
- ORR by RECICL
- OS
- Safety

- **The combination of TACE and lenvatinib (12 mg once daily ≥ 60 kg and 8 mg once daily < 60 kg) was applied and continued until the event specified in the PFS definition occurred.**
  - ✓ **TACE(cTACE) should be repeated on demand once the specified TACE criteria was met.**
  - ✓ **Tumor assessment should be done 4 weeks after first TACE and then every 8 weeks.**

［レンバチニブ添付文書抜粋］
4．効能または効果：切除不能な肝細胞癌
5．効能又は効果に関連する注意：5．3 局所療法（経皮的エタノール注入療法、ラジオ波焼灼療法、マイクロ波凝固療法、肝動脈塞栓療法／肝動脈化学塞栓療法、放射線療法等）の適応となる肝細胞癌患者に対する本剤の有効性及び安全性は確立していない。

Kudo M, et al. Liver Cancer 2023.

Tumor responses (per RECICL) in subjects

ORR of LEN+TACE

Tumor response (Patient N=62)	CR, n (%)	PR, n (%)	SD, n (%)	PD, n (%)	ORR, n (%) (90% CI)
4 weeks after first TACE [a]	33 (53.2)	16 (25.8)	4 (6.5)	2 (3.2)	49 (79.0) (68.7 – 87.1)
Best response [b]	42 (67.7)	13 (21.0)	1 (1.6)	2 (3.2)	55 (88.7) (79.8 – 94.6)

a: Not evaluable: n=7, b: Not evaluable: n=4

DoR rate

DoR rate (n=55)	Best Response (%) PR (n=13)	Best Response (%) CR (n=42)	Overall (%)
6 months (90% CI) [a]	61.5 (36.0, 79.4)	95.1 (85.0, 98.4)	87.0 (77.1, 92.8)
12 months (90% CI) [a]	28.8 (10.4, 50.6)	57.2 (42.5, 69.5)	50.5 (38.2, 61.6)

LEN-TACE achieved 68% CR (Best response)

Duration of response was >12M in more than 50 % of patients

Kudo M, et al. Liver Cancer 2023.

TACTICS-L ORR Sub-group analysis (4 weeks after first TACE)

Category		n	ORR, n	90% CI	CR, n
Performance status, n (%)	0	59	47 (79.7%)	69.1%-87.8%	32 (54.2%)
	1	3	2 (66.7%)	13.5%-98.3%	1 (33.3%)
Etiology, n (%)	Hepatitis B	8	6 (75.0%)	40.0%-95.4%	5 (62.5%)
	Hepatitis C	20	15 (75.0%)	54.4%-89.6%	9 (45.0%)
	Non-B Non-C	31	25 (80.6%)	65.3%-91.2%	16 (51.6%)
Child-Pugh score, n (%)	5	51	43 (84.3%)	73.5%-91.9%	30 (58.8%)
	6	11	6 (54.5%)	27.1%-80.0%	3 (27.3%)
AFP, n (%)	<200 ng/mL	52	42 (80.8%)	69.6%-89.2%	28 (53.8%)
	≥200 ng/mL	10	7 (70.0%)	39.3%-91.3%	5 (50.0%)
Milan criteria, n (%)	Within	28	22 (78.6%)	62.0%-90.2%	18 (64.3%)
	Outside	34	27 (79.4%)	64.8%-89.9%	15 (44.1%)
Up to 7 criteria, n (%)	Within	40	30 (75.0%)	61.3%-85.8%	22 (55.0%)
	Outside	22	19 (86.4%)	68.4%-96.2%	11 (50.0%)
	A	25	18 (72.0%)	53.8%-86.1%	16 (64.0%)
	B2	22	19 (86.4%)	68.4%-96.2%	11 (50.0%)
Prior TACE, n (%)	0	35	29 (82.9%)	68.9%-92.3%	19 (54.3%)
	1-2	26	19 (73.1%)	55.3%-86.6%	14 (53.8%)

Regardless of Up-to-7 in/out, CR rate was >50%

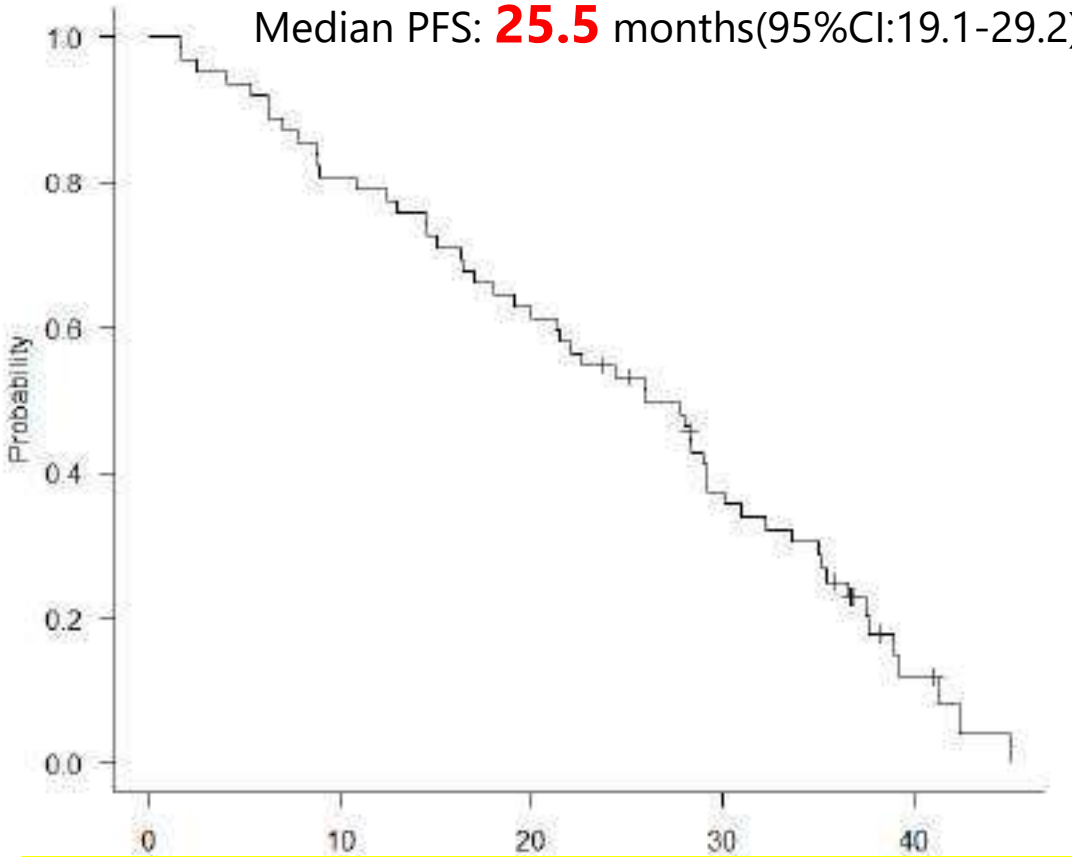
Etiology: unknown n=3, Prior TACE: unknown n=1

Kudo M, et al. Liver Cancer 2023.

Results of the interim follow-up analysis

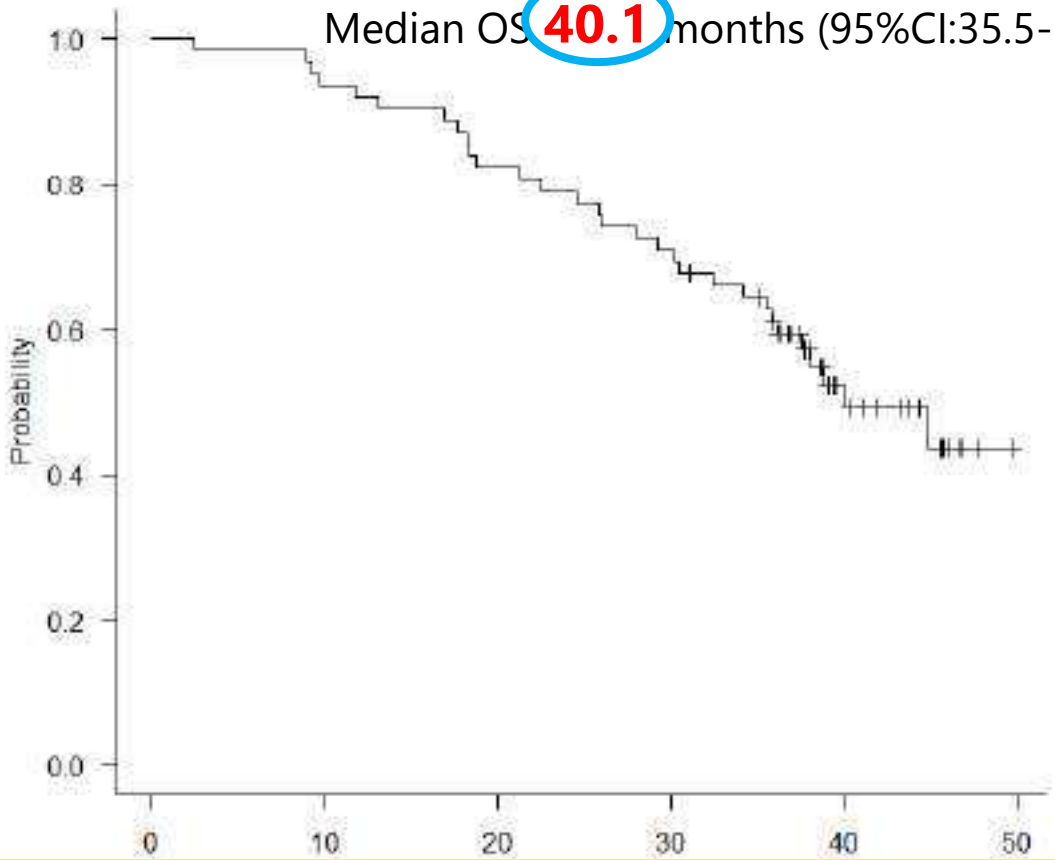
PFS

Median PFS: **25.5** months(95%CI:19.1-29.2)



OS

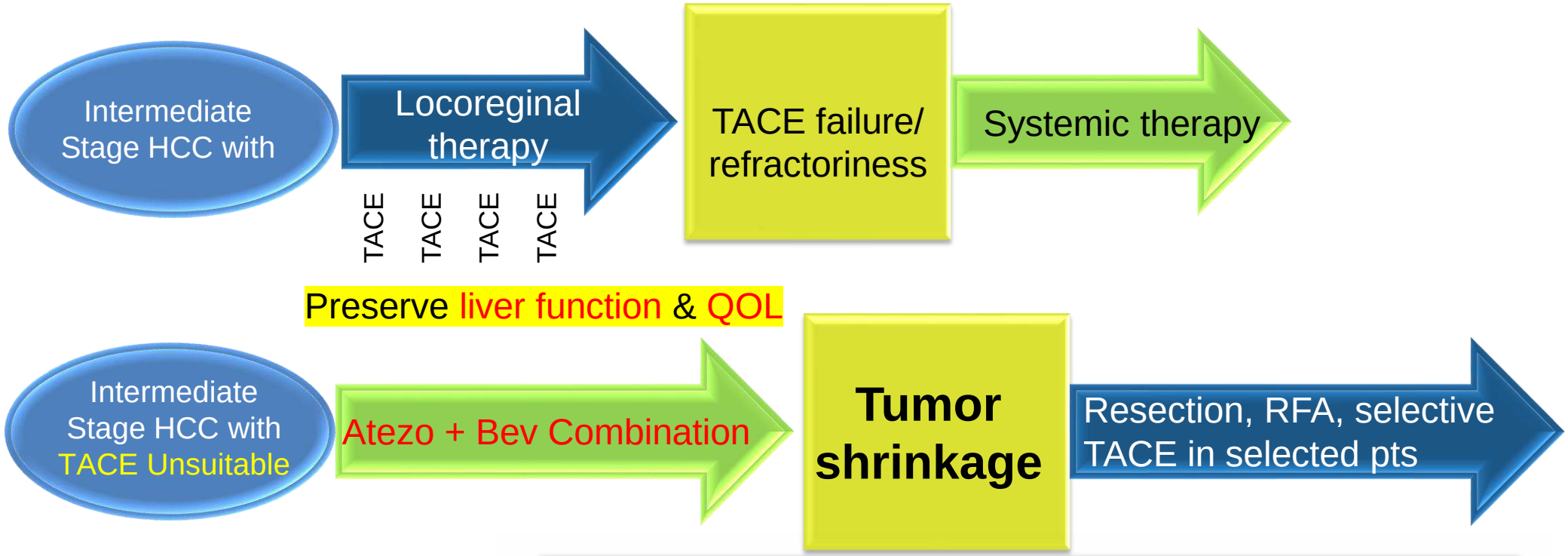
Median OS **40.1** months (95%CI:35.5-NA)



OS of 40.1 months in Intermediate-stage HCC is the longest in Prospective Trial.

Data cutoff, Apr 2023
Unpublished data

Atezo+Bev Curative Conversion Therapy



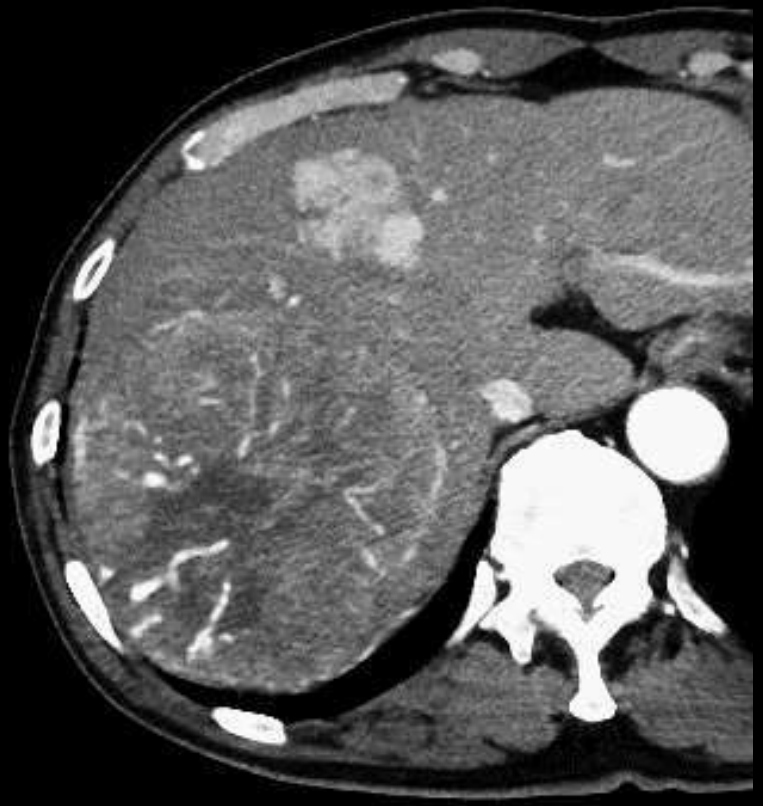
"ABC-Conversion therapy"

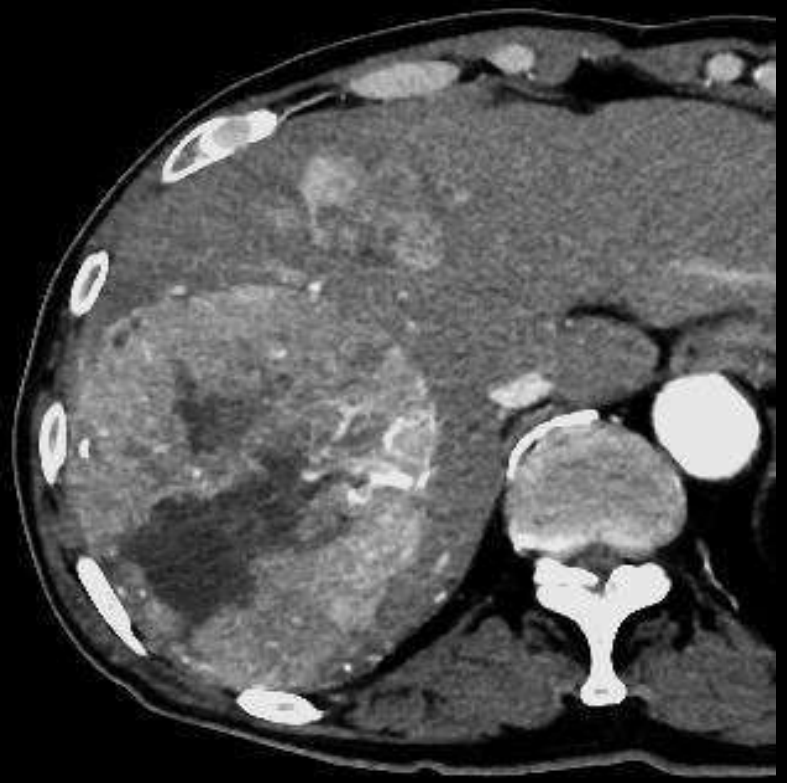
Cancer free with drug free

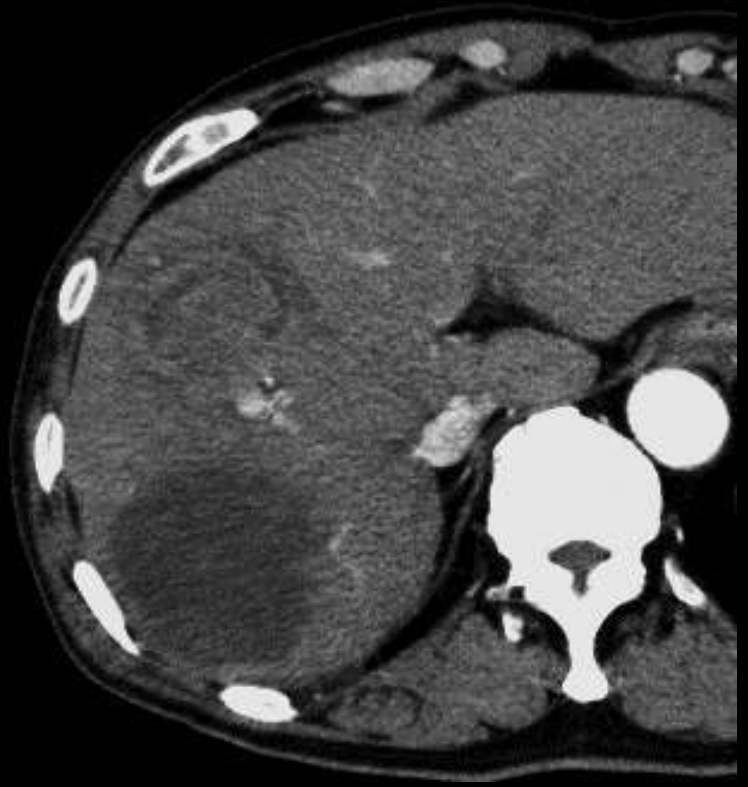
Kudo M et al, Liver Cancer 9: 367-377, 2020.

70s, NASH, BCLCB
S5: 45 mm, S7: 125 mm, Atz/Bev

Baseline	6 week	12 week
	mRECIST / RECISTv1.1	mRECIST / RECISTv1.1
S5: 45 mm	SD / SD	PR / SD
S7: 125 mm	Pseudoprogression like / SD	PR / PR



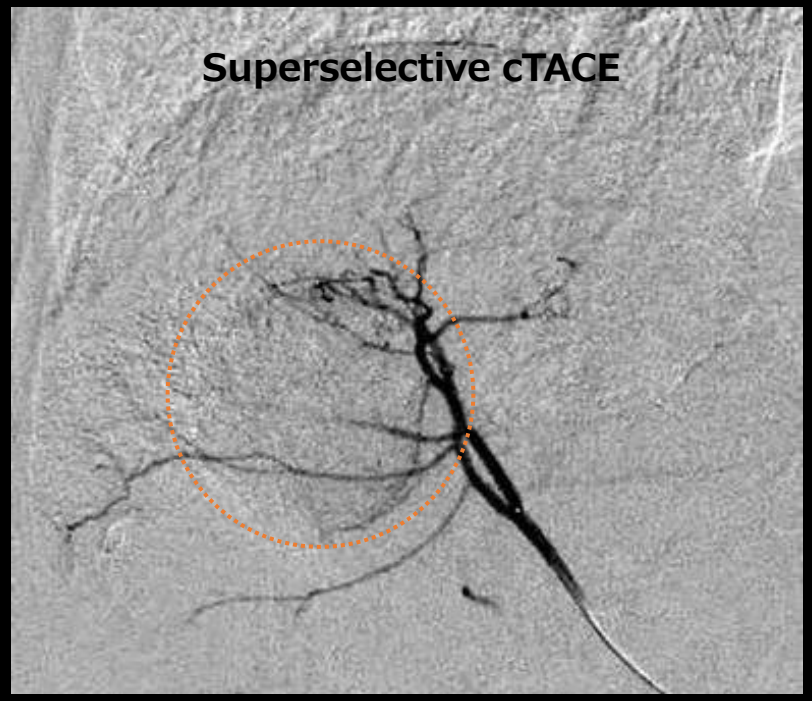




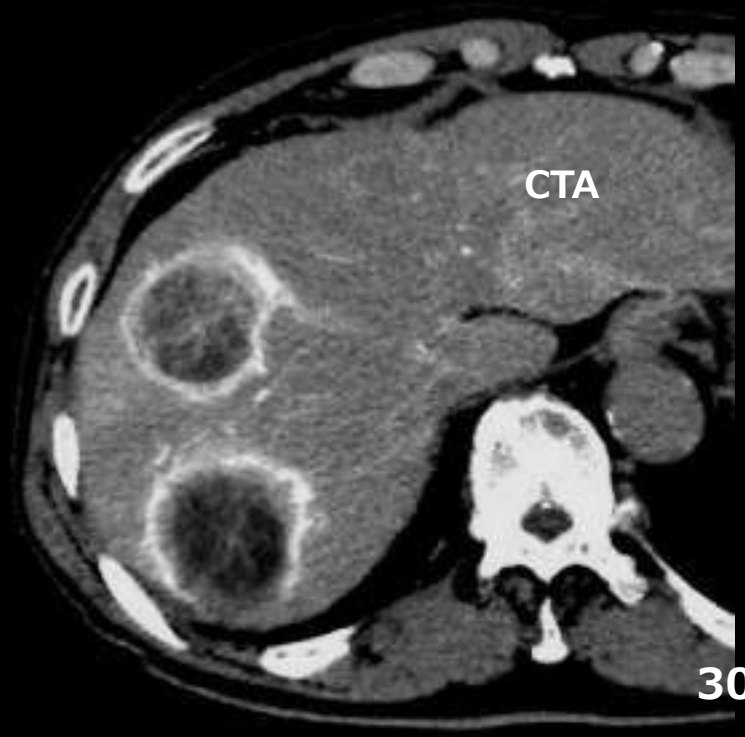
Courtesy: Dr. Abe and Kuroda, Iwate Medical University

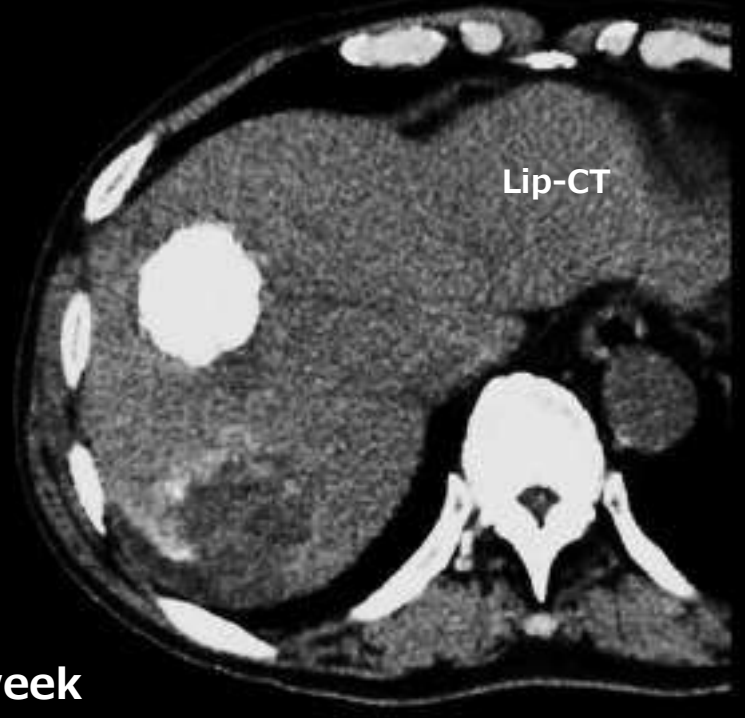
70s, NASH, BCLCB
S5: 45 mm, S7: 125 mm, Atz/Bev
conventional TACE

	6 week	12 week	30 week
	mRECIST / RECISTv1.1	mRECIST / RECISTv1.1	RECICL
S5: 45 mm	SD / SD	PR / SD	CR
S7: 125 mm	Pseudoprogression like / SD	PR / PR	PR



28 week





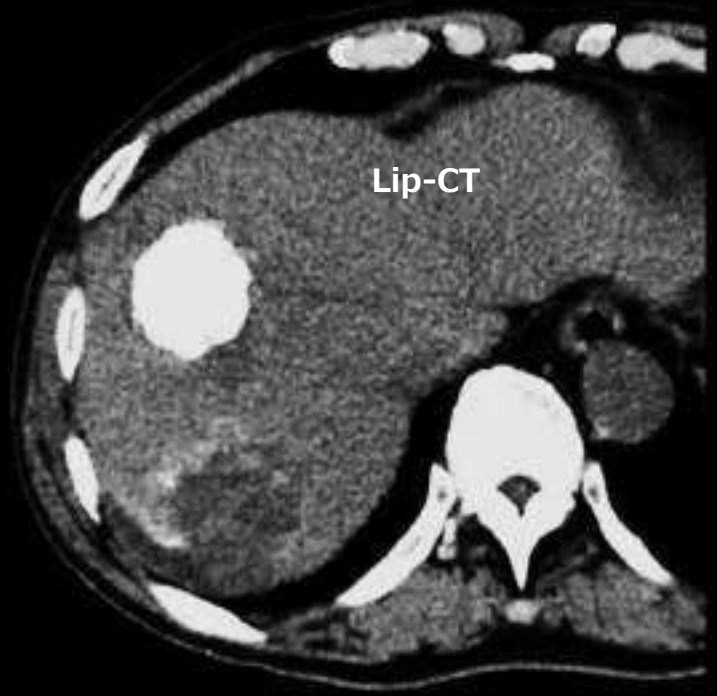
30 week

Courtesy: Dr. Abe and Kuroda, Iwate Medical University

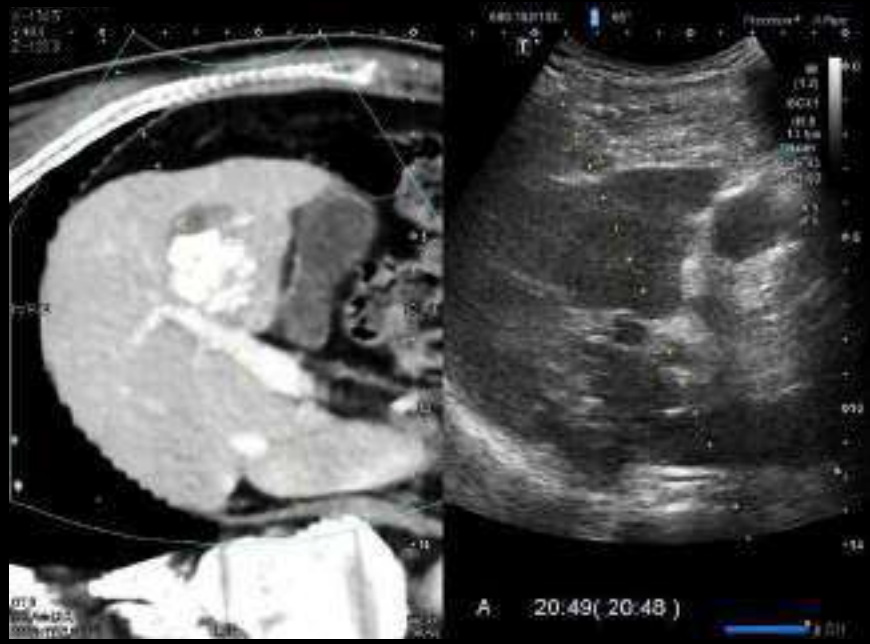
70s, NASH, BCLCB
S5: 45 mm, S7: 125 mm, Atz/Bev
ABC conversion(MWA) → Drug free

	6 week	12 week	30 week	48 week
	mRECIST / RECISTv1.1	mRECIST / RECISTv1.1	RECICL	RECICL
S5: 45 mm	SD / SD	PR / SD	CR	CR
S7: 125 mm	Pseudoprogression like / SD	PR / PR	PR	CR

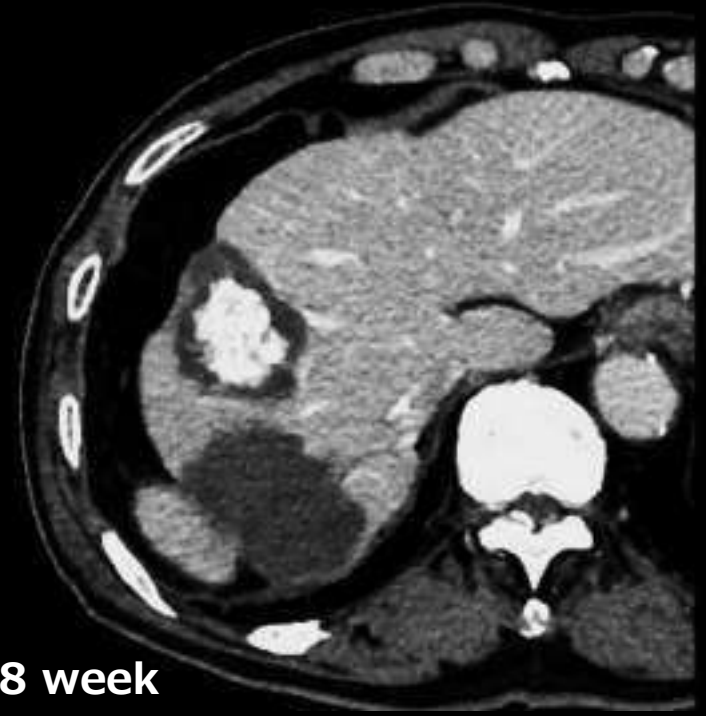
Microwave Ablation



30 week



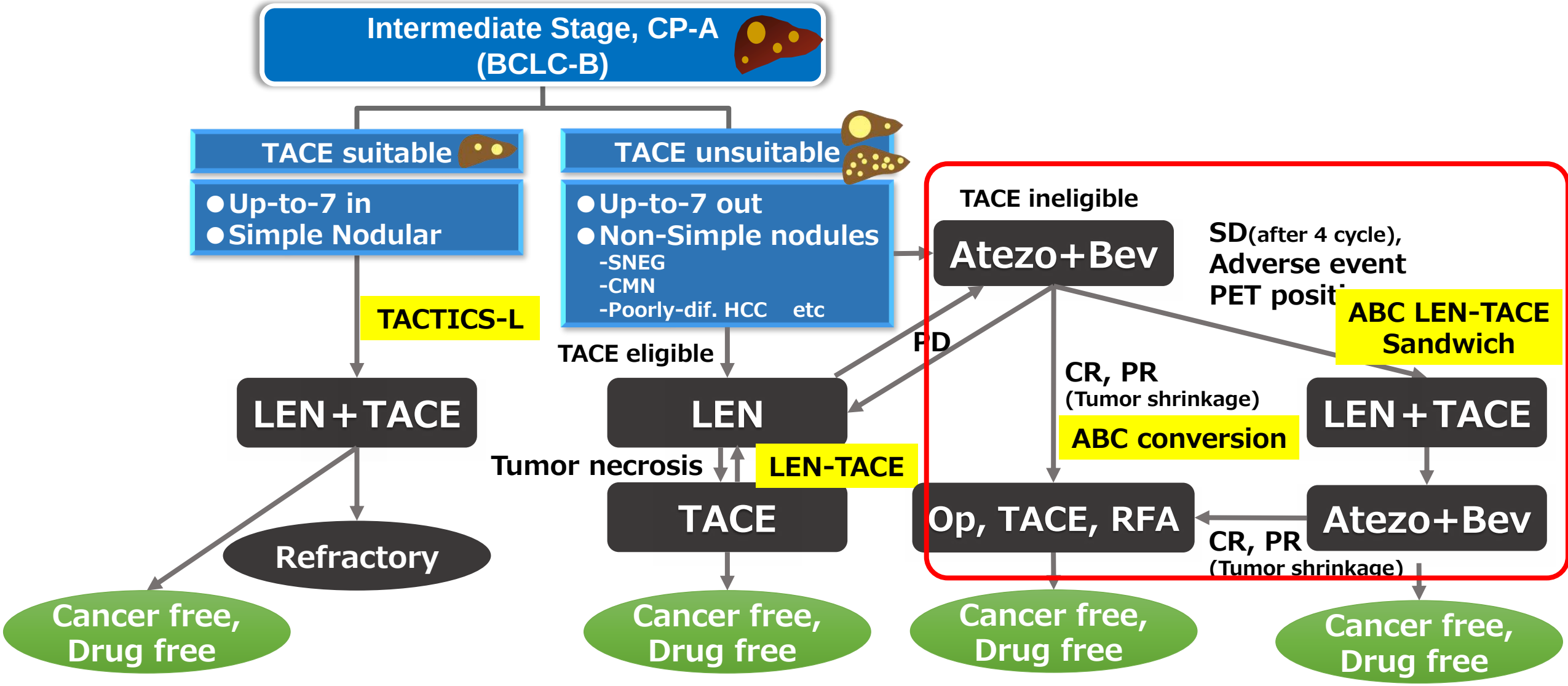
40 week



48 week

Courtesy: Dr. Abe and Kuroda, Iwate Medical University

Treatment Strategy for Intermediate stage HCC

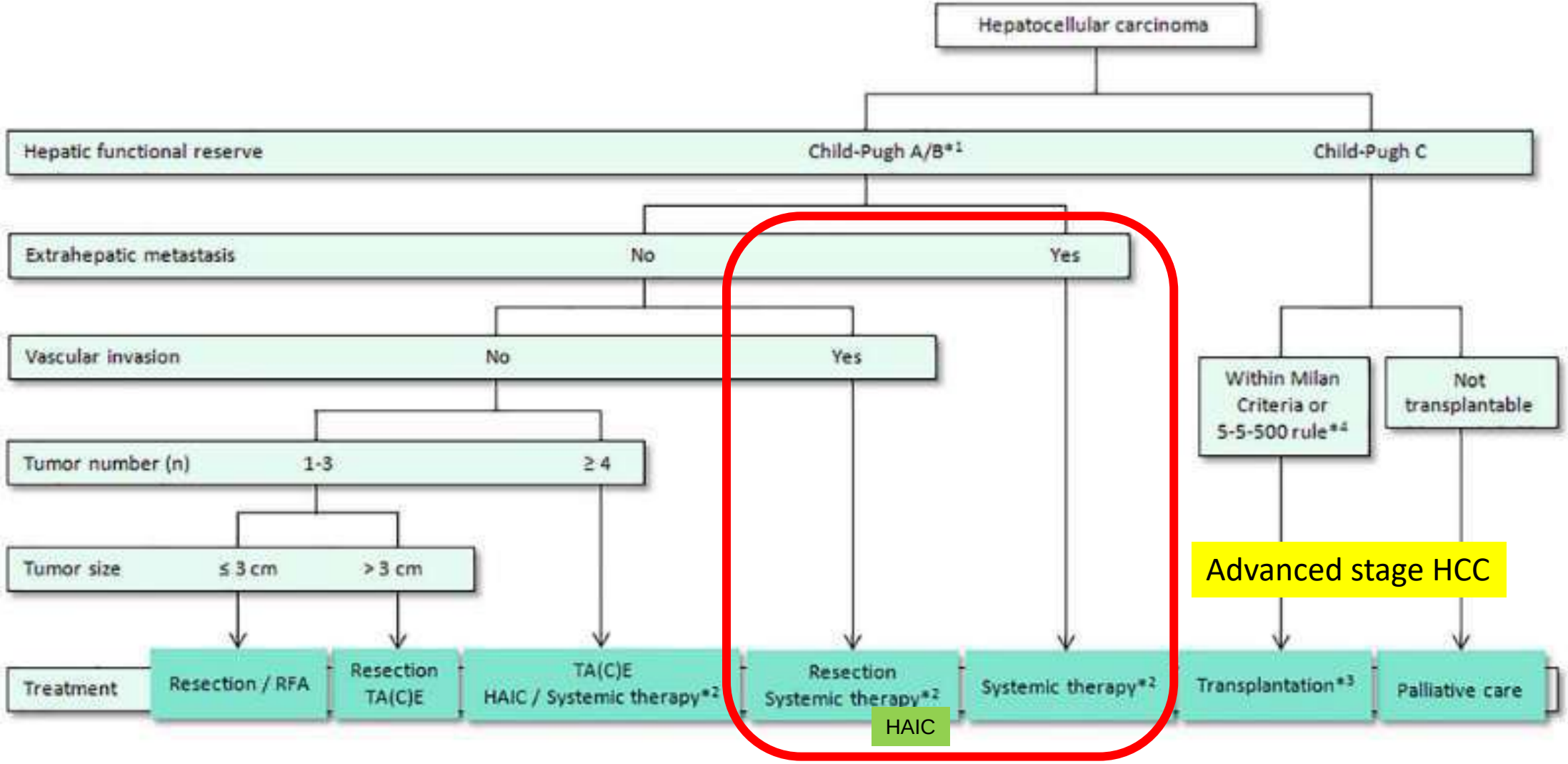


Kudo M. Int J Clin Oncol 2022.

Outline

- Overview of HCC trend in Japan
- Overview of HCC outcome in Japan
- Overview of HCC surveillance in Japan
- Innovative treatment strategy in Early-stage HCC
- Innovative treatment strategy in Intermediate-stage HCC
- Innovative treatment strategy in Advanced stage HCC
- Role of Multidisciplinary Team
- Lessons learned from Japan’s experience
- Future innovations and Personalized Medicine

JSH HCC Guidelines 2021 Algorithm for Treatment



Hasegawa K, Tateishi R, Kudo M, et al. Hepatol Res. 2023

History of Drug Approval in HCC in Japan

1stLine

2ndLine

2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2022 2023

SHARP, Asia Pacific

Sorafenib

REFLECT

Lenvatinib

IMbrave150

Atezolizumab
+Bevacizumab

HIMALAYA

Durvalumab
+ Tremelimumab

Durvalumab

Regorafenib

RESORCE

Ramucirumab

REACH-2

Cabozantinib

CELESTIAL

JSH-HCC Guidelines: Algorithm for systemic therapy

Hepatocellular carcinoma

Advanced HCC not indicated for resection, transplantation, RFA, TA(C)E, etc.
Good performance status and Child-Pugh A liver function

Indication for combination immunotherapy

Yes

1st line

- **Atezolizumab＋Bevacizumab**
- **Tremelimumab＋Durvalumab**

2nd line or later

- ・Sorafenib
  ・Lenvatinib
  ・Regorafenib
  ・Ramucirumab
  ・Cabozantinib
  ・Tremelimumab ＋Durvalumab
  ・Durvalumab
- ・Sorafenib
  ・Lenvatinib
  ・Regorafenib
  ・Ramucirumab
  ・Cabozantinib
  ・Atezolizumab＋Bevacizumab

No

1st line

- **Sorafenib**
- **Lenvatinib**
- **Durvalumab**

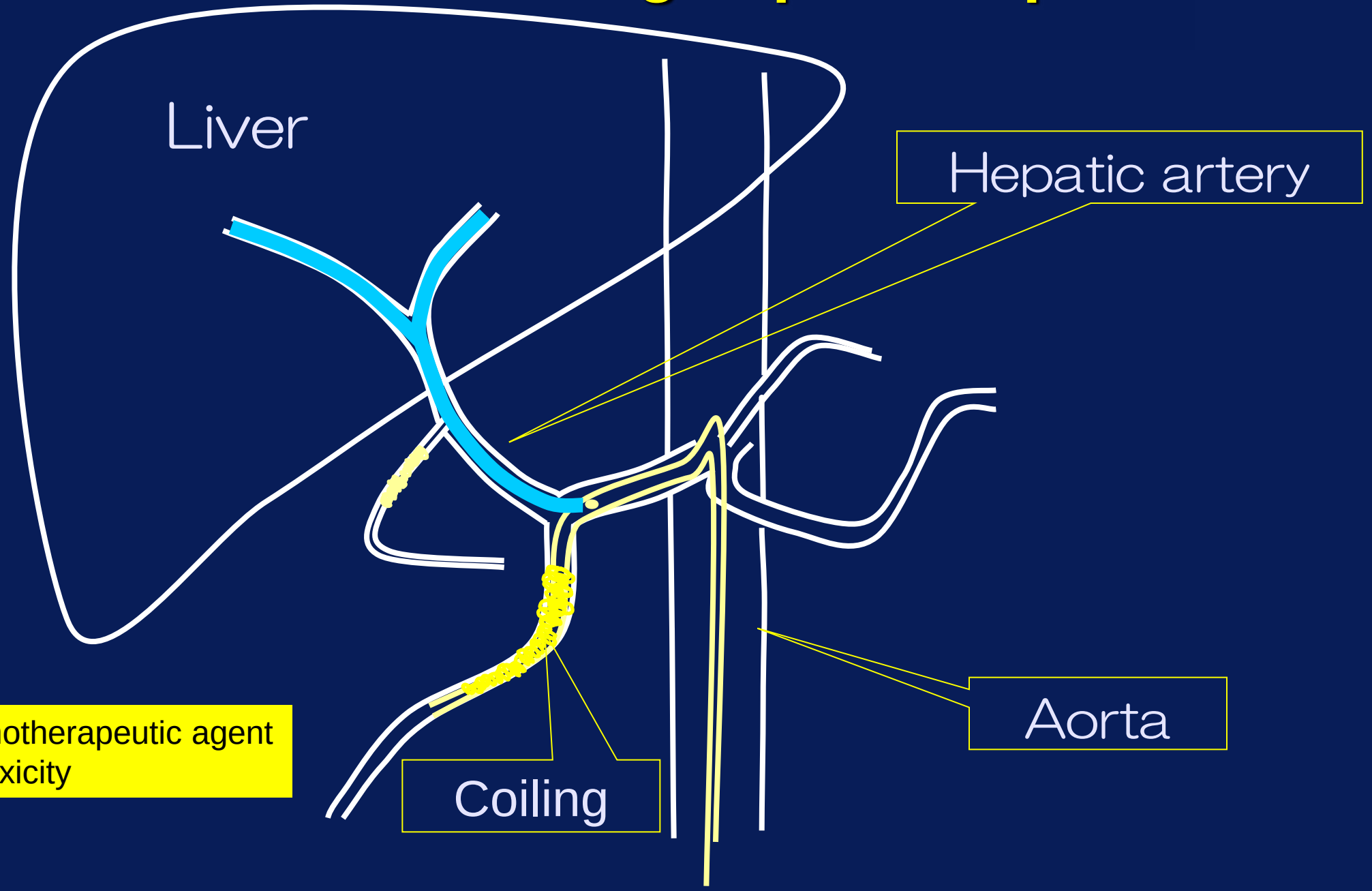
2nd line or later

- ・**Regorafenib**
  ・**Ramucirumab**
  ・**Cabozantinib**
  ・Lenvatinib
- ・Sorafenib
  ・Regorafenib
  ・Ramucirumab
  ・Cabozantinib
- ・Sorafenib
  ・Regorafenib
  ・Lenvatinib
  ・Ramucirumab
  ・Cabozantinib

Bold face with underline indicates the availability of evidence from randomized controlled trials.

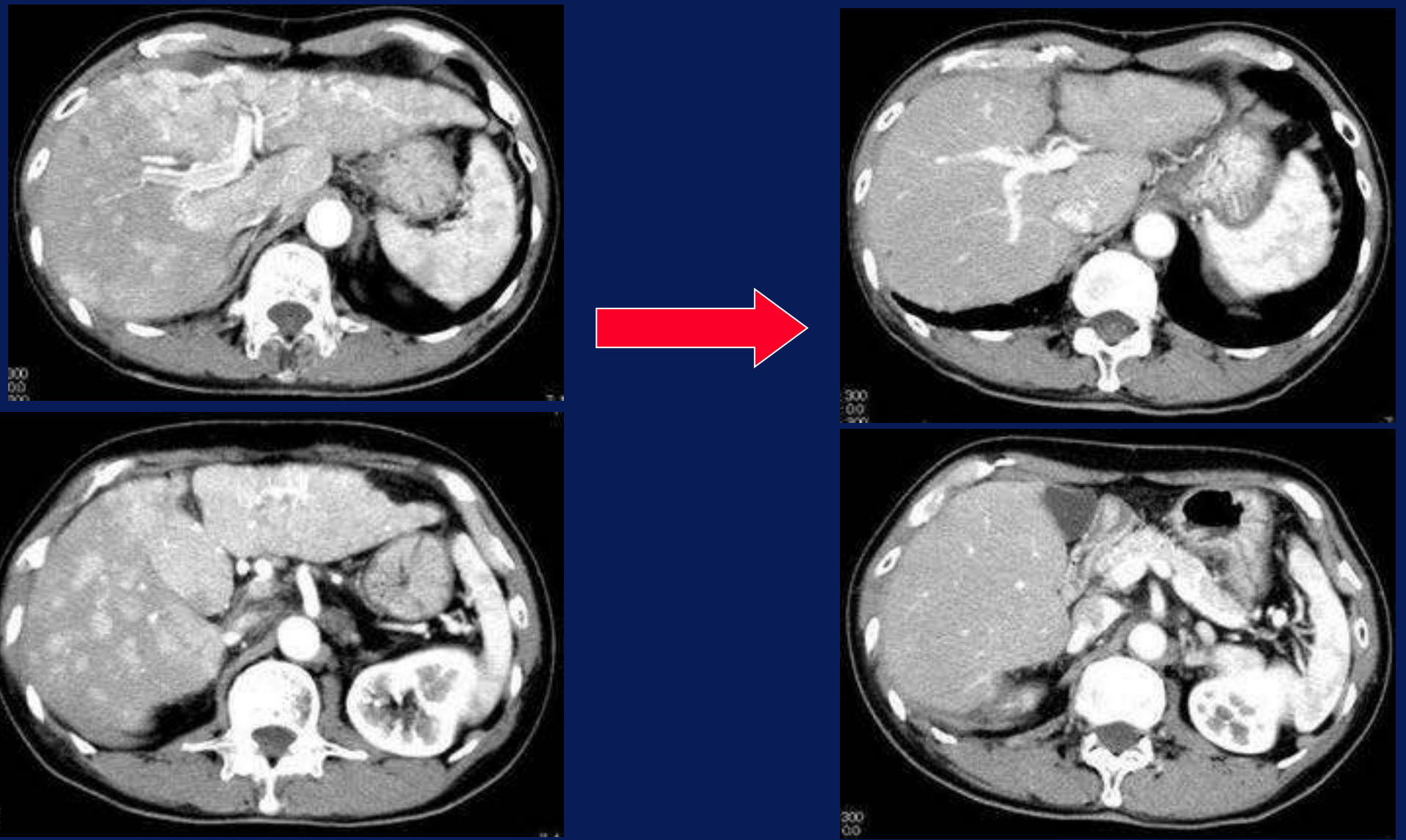
JSH Clinical Practice Guideline for HCC 2023.

Continuous HAIC using implanted port



- ✓ High dose chemotherapeutic agent
- ✓ Low systemic toxicity

Continuous HAIC with implanted port

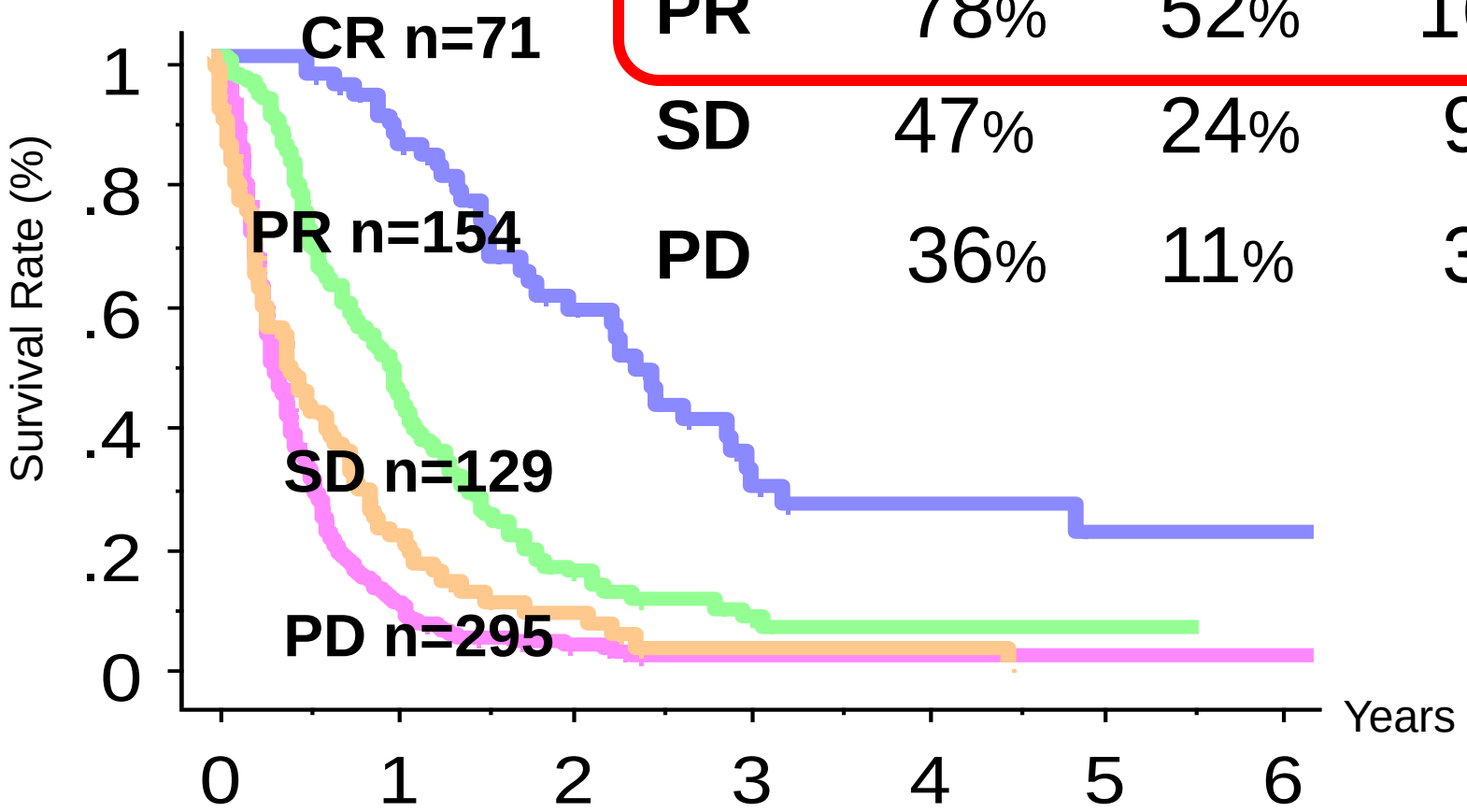


HAIC Efficacy

(n=649)

Effective for PVTT

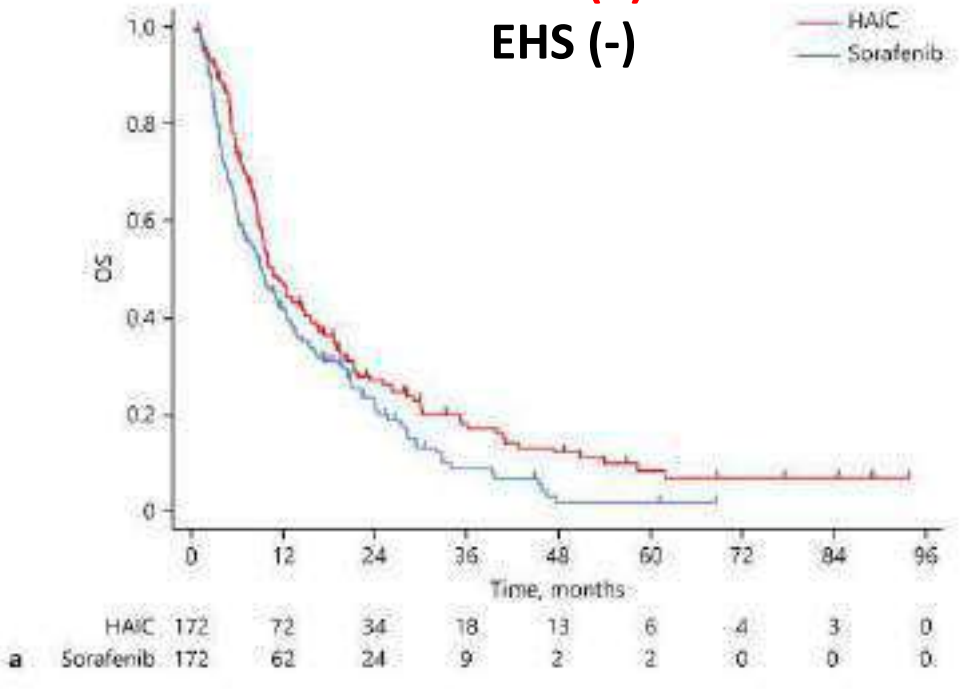
	0.5y	1y	2y	MST
CR	100%	91%	61%	**28.9 M**
PR	78%	52%	16%	**12.2 M**
SD	47%	24%	9%	**5.5 M**
PD	36%	11%	3%	**4.3 M**



HAICvs Sorafenib

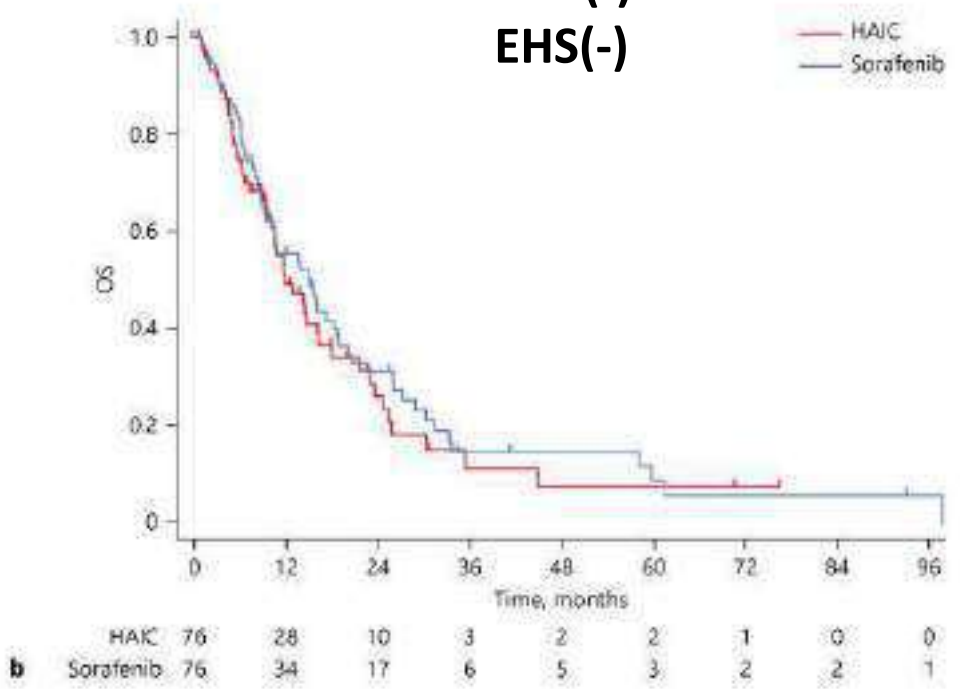
-PSM study-

MVI (+)
EHS (-)



HAIC: 10.6 months [95% CI 9.1–14.3]
Sorafenib: 9.1 months [95% CI 6.8–12.0]
HR: 0.667 [95% CI 0.475–0.935]
***p* = 0.018**

MVI(-)
EHS(-)



HAIC: 12.2 months [95% CI 9.9–16.5]
Sorafenib: 15.4 months [95% CI 9.7–19.1]
HR: 1.227 [95% CI 0.699–2.155]
***p* = 0.475**

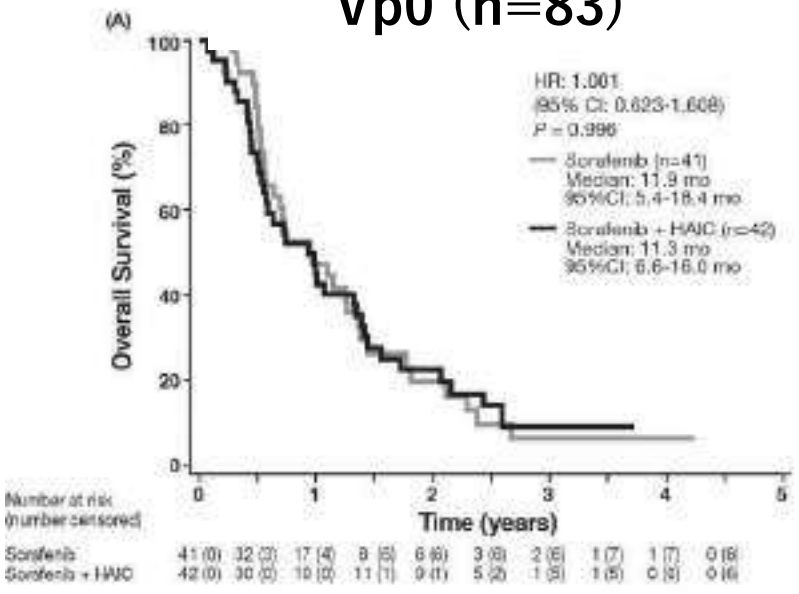
HAIC is effective for PVTT

Ueshima K, Kudo M et al. Liver Cancer. 2020;9(5):583-95.

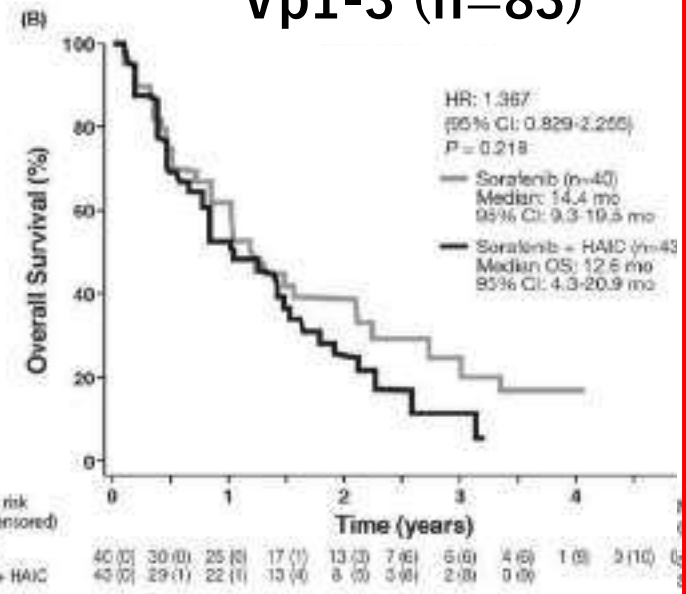
Phase 3 SILIUS Trial: OS sub-analysis

Sorafenib vs. Sorafenib plus HAIC (Low-dose FP)

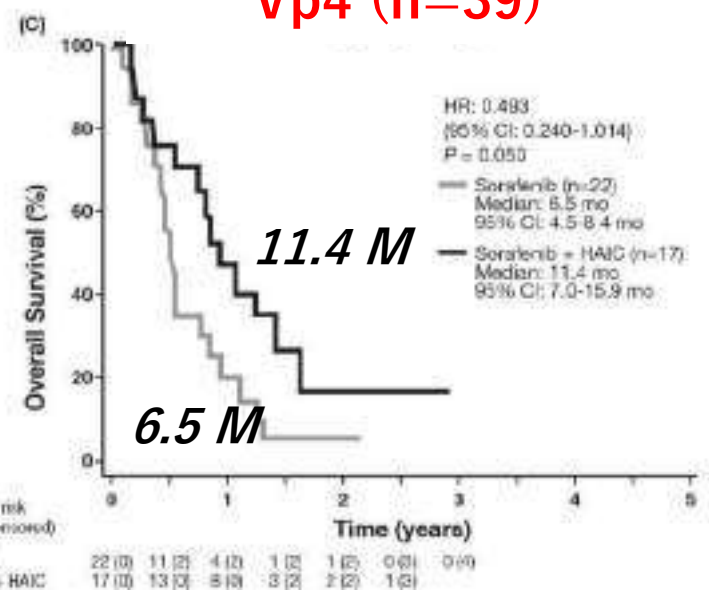
Vp0 (n=83)



Vp1-3 (n=83)



Vp4 (n=39)



HAIC is still performed in pts with MVI (Vp3/4) in Japan.

HAIC is effective for Vp4 patients

Kudo M, et al. Lancet Gastroenterol Hepatol 2018

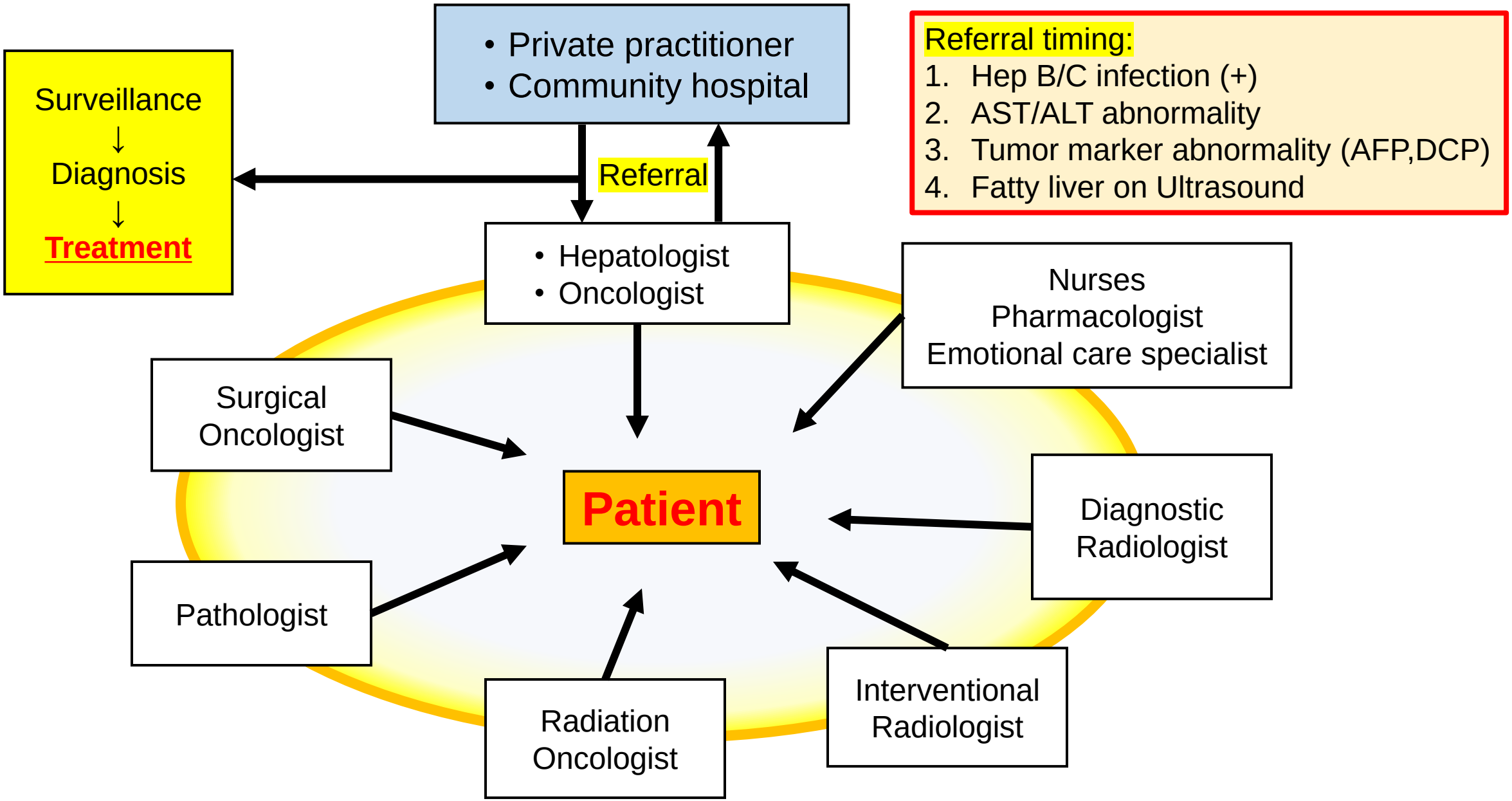
In Japan,

All patients can **easily access these high quality, sophisticated treatments** including resection, transplantation, ablation, superselective TACE, combination of systemic and locoregional therapy and combination Immunotherapy at referral institute in all over Japan by fully covered insurance

Outline

- Overview of HCC trend in Japan
- Overview of HCC outcome in Japan
- Overview of HCC surveillance in Japan
- Innovative treatment strategy in Early-stage HCC
- Innovative treatment strategy in Intermediate-stage HCC
- Innovative treatment strategy in Advanced stage HCC
- Role of Multidisciplinary Team
- Lessons learned from Japan’s experience
- Future innovations and Personalized Medicine

Role of Multidisciplinary Team: Patient-centered Care



Outline

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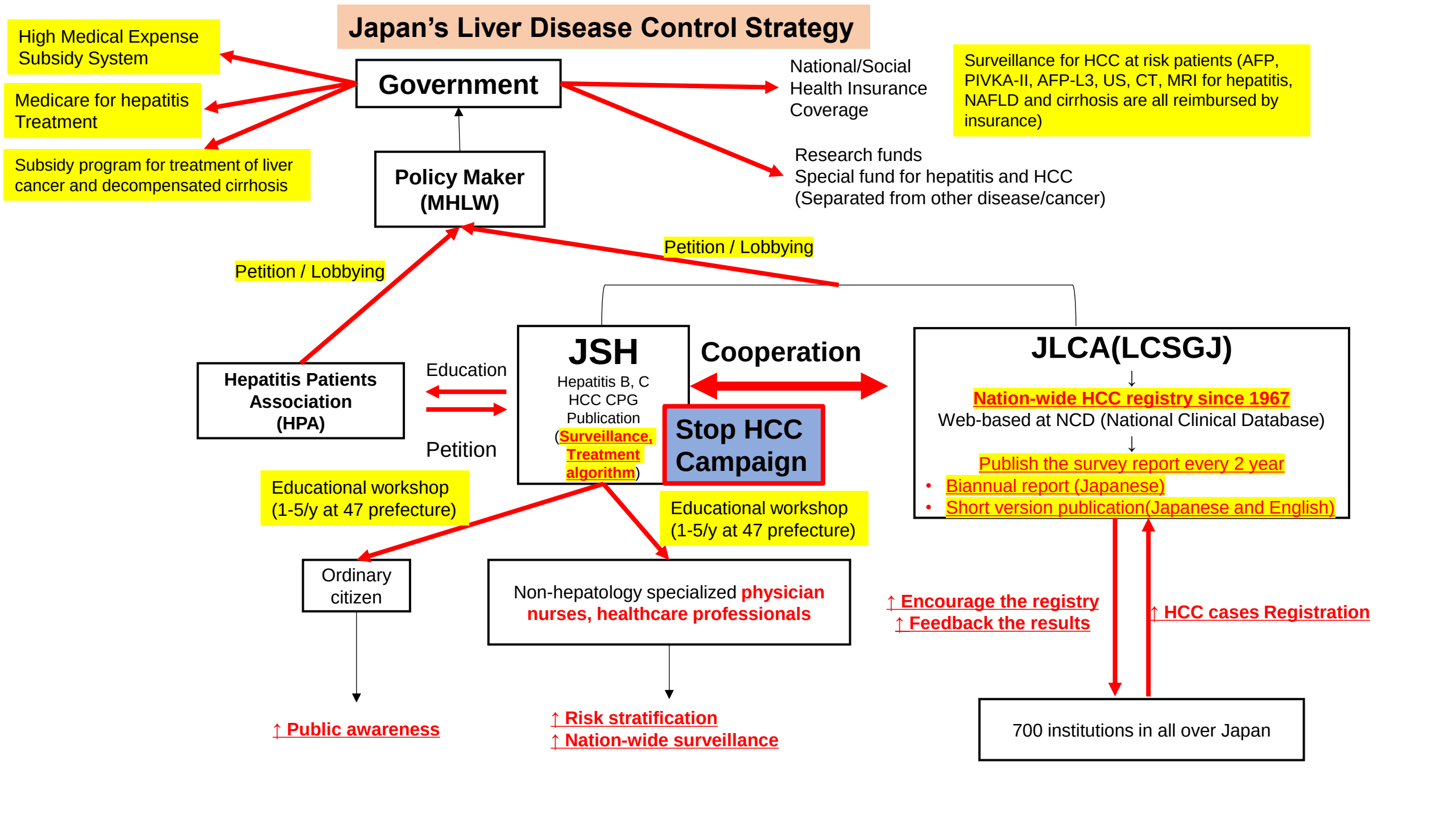
Japan's Liver Disease Control Strategy
High Medical Expense Subsidy System
Medicare for hepatitis Treatment
Subsidy program for treatment of liver cancer and decompensated cirrhosis
Government
National/Social Health Insurance Coverage
Surveillance for HCC at risk patients (AFP, PIVKA-II, AFP-L3, US, CT, MRI for hepatitis, NAFLD and cirrhosis are all reimbursed by insurance)
Research funds
Special fund for hepatitis and HCC
(Separated from other disease/cancer)
Policy Maker (MHLW)
Petition / Lobbying
Petition / Lobbying
Hepatitis Patients Association (HPA)
Education
Petition
JSH
Hepatitis B, C HCC CPG Publication (Surveillance, Treatment algorithm)
Cooperation
Stop HCC Campaign
JLCA(LCSGJ)
Nation-wide HCC registry since 1967
Web-based at NCD (National Clinical Database)
Publish the survey report every 2 year
Biannual report (Japanese)
Short version publication(Japanese and English)
Educational workshop (1-5/y at 47 prefecture)
Educational workshop (1-5/y at 47 prefecture)
Ordinary citizen
Non-hepatology specialized physician nurses, healthcare professionals
↑ Encourage the registry
↑ Feedback the results
↑ HCC cases Registration
↑ Public awareness
↑ Risk stratification
↑ Nation-wide surveillance
700 institutions in all over Japan

Outline

- Overview of HCC trend in Japan
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- Innovative treatment strategy in Advanced stage HCC
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- Lessons learned from Japan’s experience
- Future innovations and Personalized Medicine

Lack of human resources or medical equipment, resulting in a failure of early HCC detection

Introducing AI to the medical / healthcare field

A solution for a luck of manpower in the aging society

Utilization of existing medical data

AI = quick processing and correct output

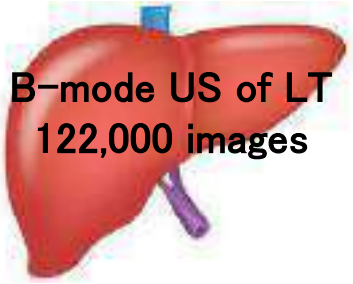
✓ Improvement work efficiency

✓ Improvement the quality

Reduce the burden of patients and healthcare professionals

Construction of nationwide database for US digital images

AI for diagnosis of liver tumor

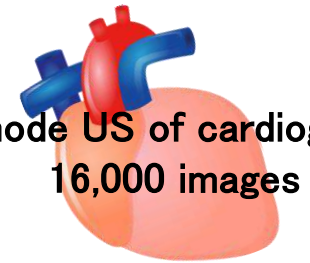


B-mode US of LT
122,000 images

AI for diagnosis of mammary tumor

B-mode US of MT
20,000 images

AI for diagnosis of heart disease



B-mode US of cardiography
16,000 images

JSUM

Cent. Data Sarver

National Institute of Informatics

Data transfer to central server
Automated anonymization

SINET, VPN

Curation and upload system

Image
Additional inf

2 …… 11

11 institutions

US, report & image filing system

Abdominal US Group

Curation and upload system

Image
Additional inf

2 …… 5

5 institutions

US, report & image filing system

Mammary US group

Curation and upload system

Image
Additional inf

2 …… 5

5 institutions

US, report & image filing system

Heart disease US group

- **Liver Tumor**
- **Mammary tumor**
- **Heart Disease**

2018. 8. ～

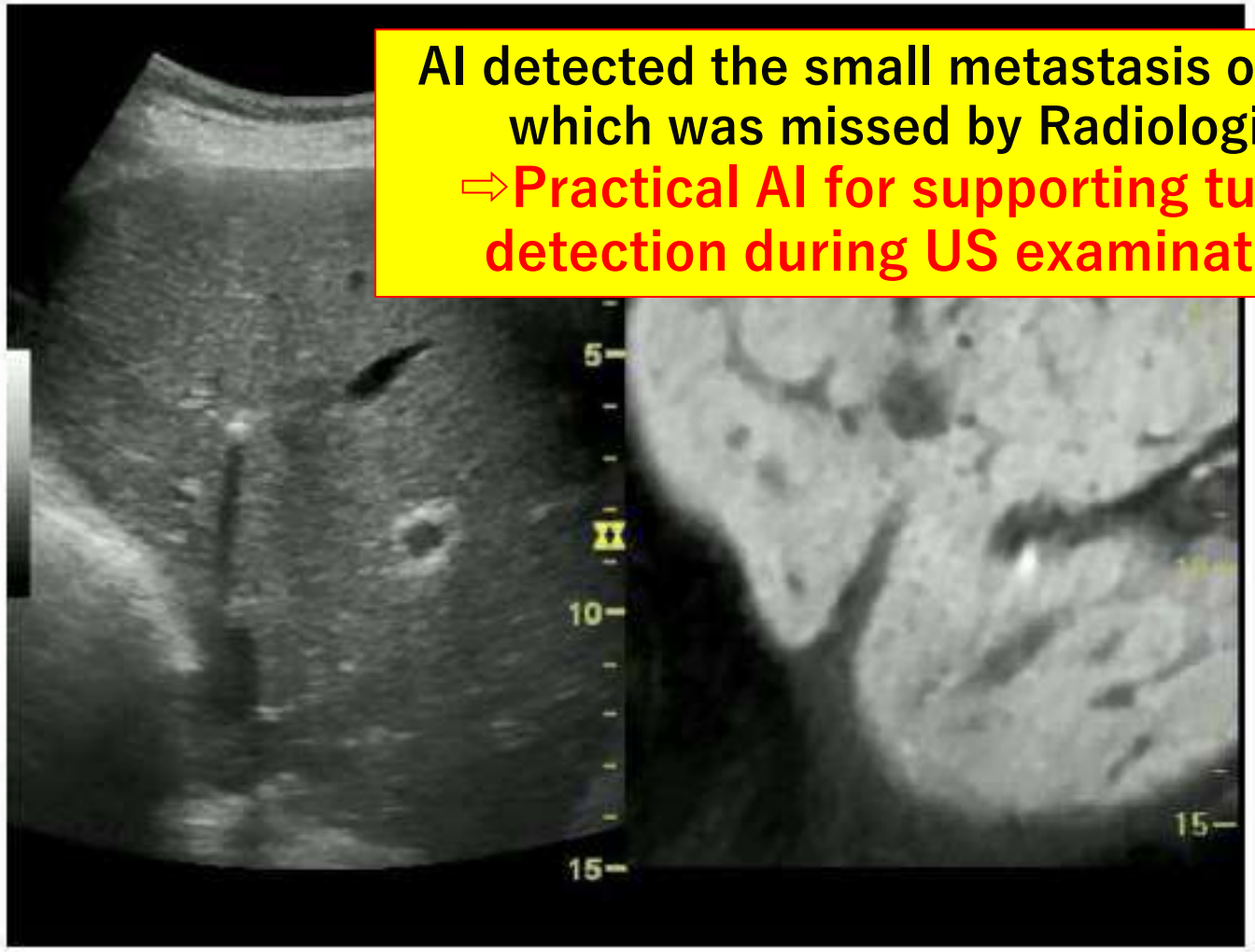
2019. 9. ～

Kudo M, et al. AMED Report 2024

Detection of small metastasis of HCC before RFA

HCC

- No. of total frames
  2,260 frames
- No. of frames with tumor
  544 frames
- Correct detection
  (+)



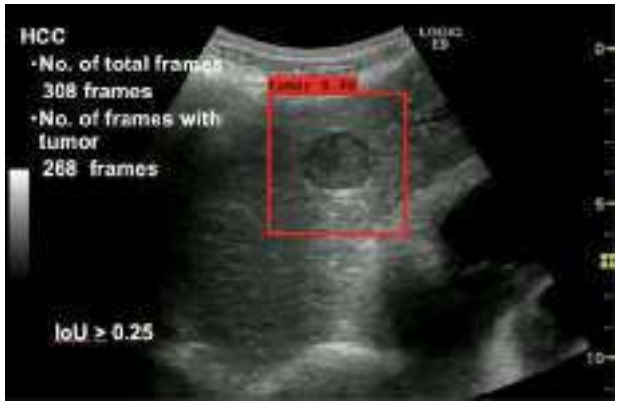
AI detected the small metastasis of HCC which was missed by Radiologist
⇨Practical AI for supporting tumor detection during US examination

Kudo M, et al. AMED Report 2024

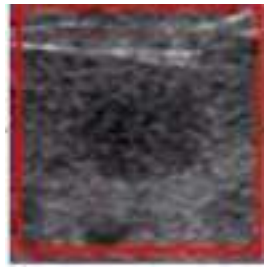
AI-powered detection and classification system

Integration of detector and classifier

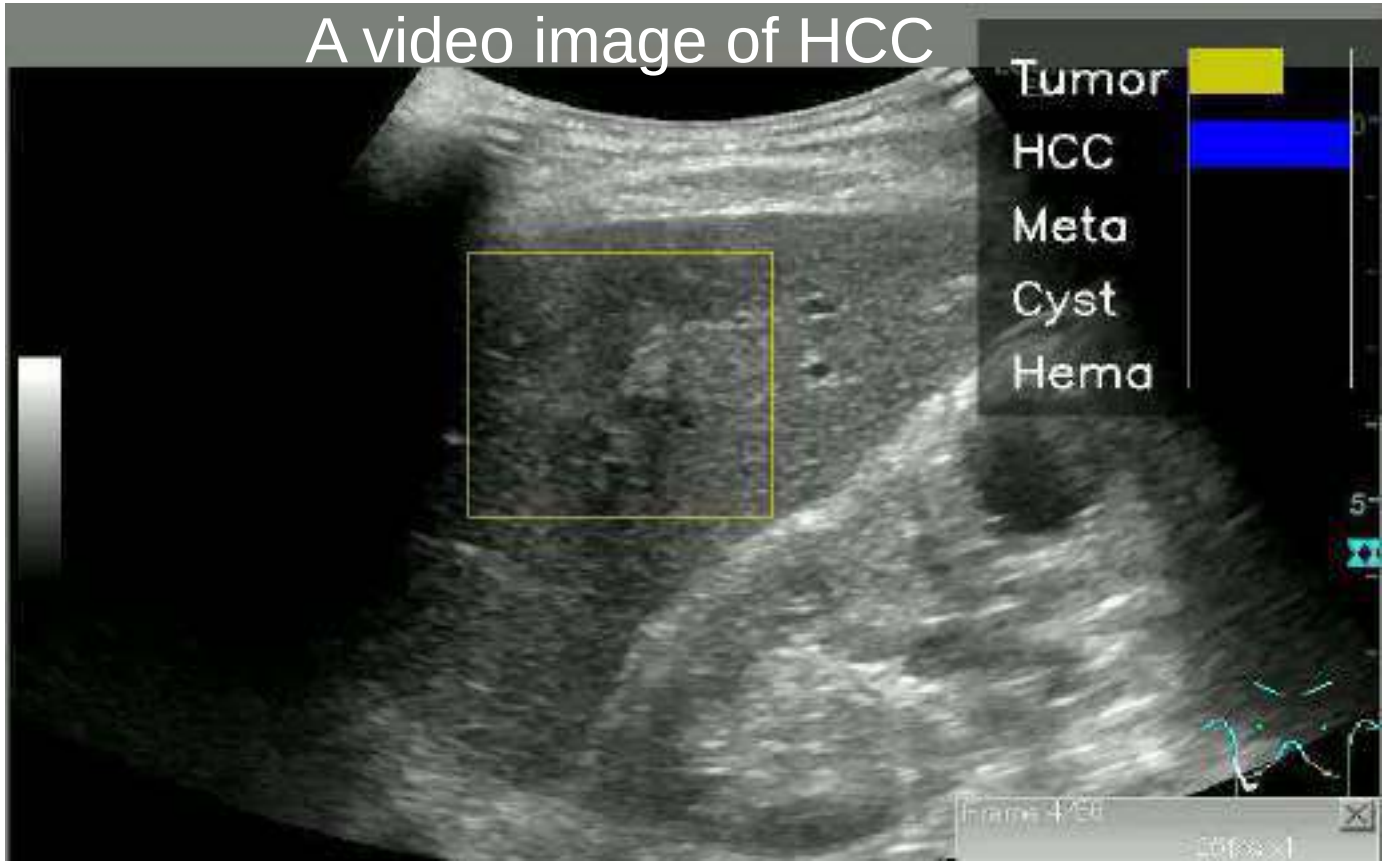
Detector of tumor
YOLO v5



Classifier of tumor
CNN_VGG19

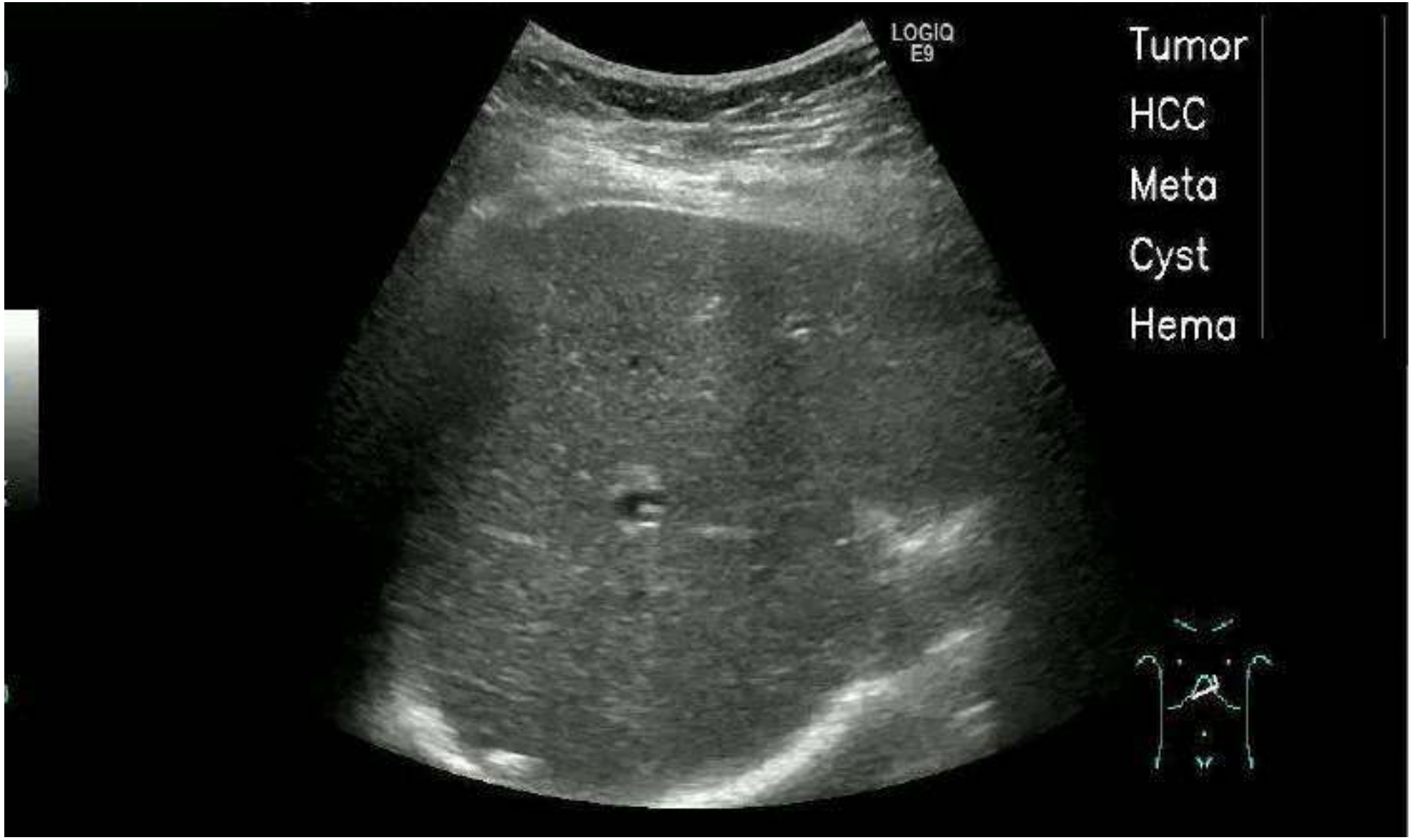


Detection and classification of liver tumor



Kudo M, et al. AMED Report 2024

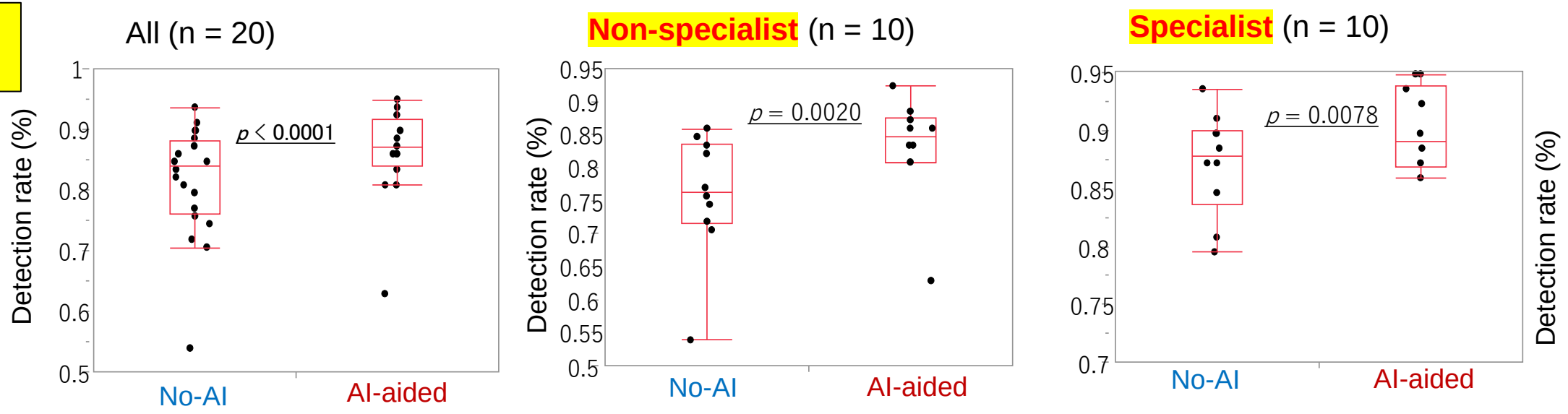
Detection and diagnosis of metastatic tumor



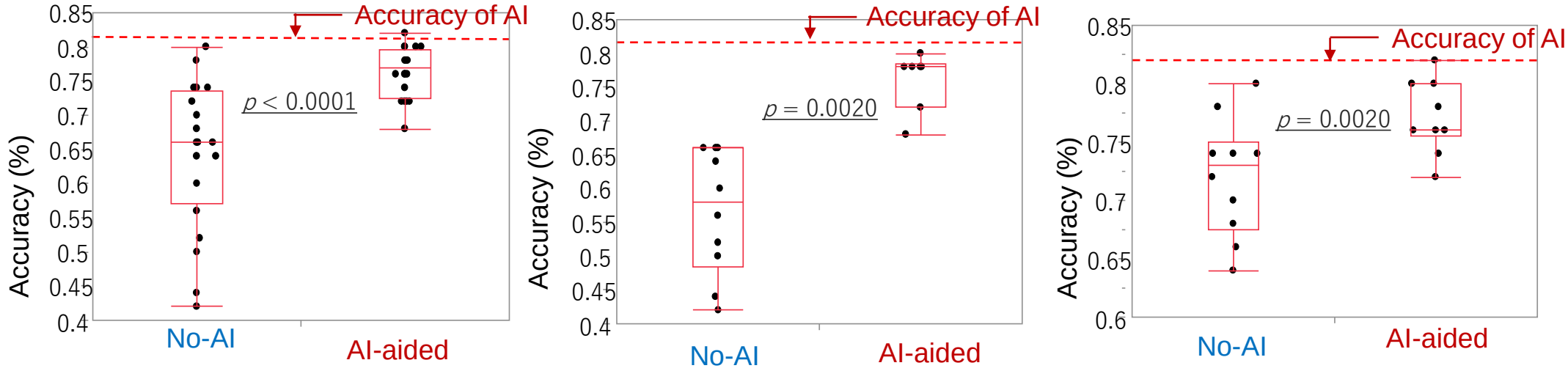
Kudo M, et al. AMED Report 2024

Efficacy of Newly Developed US AI System by JSUM

Lesion detection



Lesion diagnosis



Both lesion detection and diagnosis are improved both in non-specialist and specialist

Loadmap of Ultrasound AI system to spread to all over the world, especially to Asian countries

- ➢2018 Start this project
- ➢2021 Completion of National B-mode ultrasound database
- ➢2022 Ultrasound AI diagnostic system developed
- ➢2023 Start cooperative work with Ultrasound venders (Canon, GE and Fujifilm)
- ➢2025-6 Approval of this Ultrasound AI diagnostic system from PMDA
- ➢2026-7 The commercial US machine equipped with this AI diagnostic system will be exported to all over the world, especially to Asian courtiers (few US specialist) **for easy detection and diagnosis of small HCC**

Collaborators

Principle Investigator:

Masatoshi Kudo, **Kindai University, Japan Society of Ultrasonics in Medicine**

公益社団法人 日本超音波医学会 The Japan Society of Ultrasonics in Medicine

AI for classification

Makoto Yamakawa, Tsuyoshi Shiina: Kyoto University (Shibaura institute of Technology), **Japan Society of Ultrasonics in Medicine**

AI for detection

Yoshito Mekada: Cyukyo University

Information engineering, **Cyukyo University**

Construction of central server

Tomohiro Kuroda: Kyoto University Hospital

Database and data collection: Japan Society of Ultrasonics in Medicine

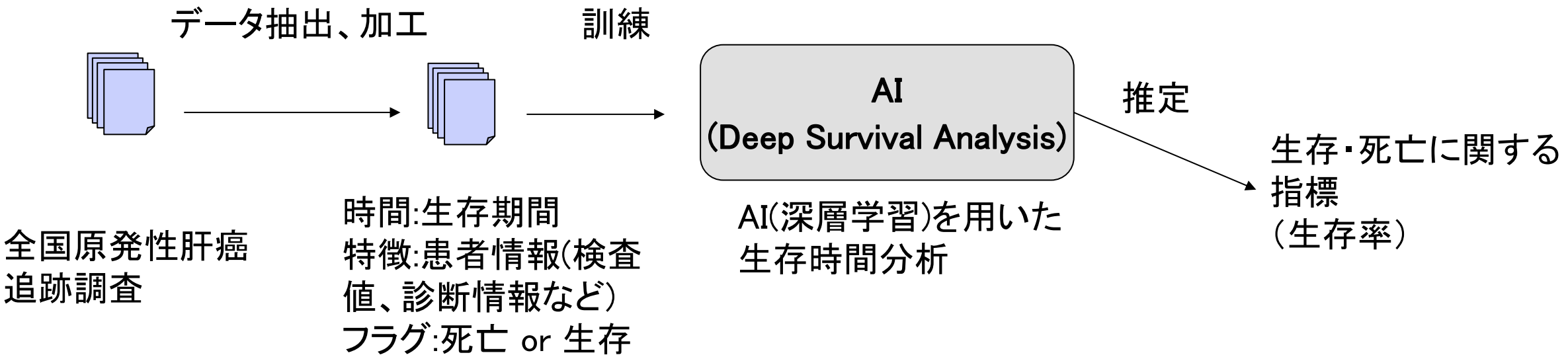
Hiroko Iijima: Hyogo Medical School
ChIikara Ogawa: Takamatsu Red-Ross Hospital
Masahiro Ogawa: Nihon University
Masayuki Kitano: Wakayama Medical University
Ken Takahashi：Kyoto University Hospital
Ryosuke Tateishi: The University of Tokyo
Hidenori Toyota: Ogaki Municipal Hospital
Naoya Sakamoto: Hokkaido University
Mutsumi Nishida: Hokkaido University Hospital
Toshiko Hirai: Nara Medical University
Hideaki Mori: Teikyo University

AMED 国立研究開発法人 日本医療研究開発機構 Japan Agency for Medical Research and Development

This project is supported by the grant from Japan Agency for the Medical Research and Development (AMED).

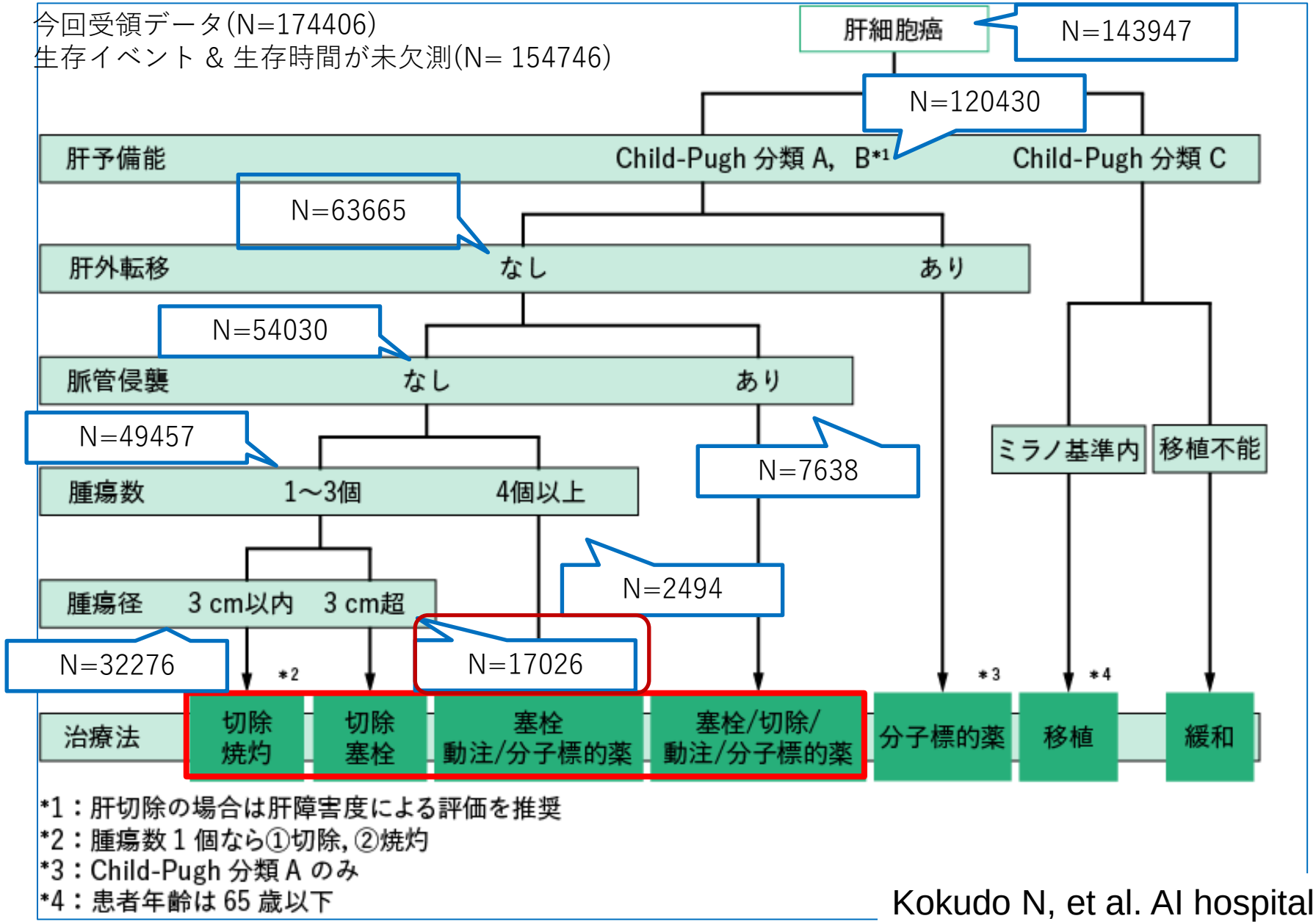
AI-aided Treatment Decision Making

AIを用いた生存時間分析を行うことで、各患者ごとの生存・死亡に関する指標(生存率)を推定できるアルゴリズムの構築・訓練を行う。



Kokudo N, et al. AI hospital Project 2024

対象集団の抽出方法および治療法の定義



Kokudo N, et al. AI hospital Project 2024

AI-based Treatment Decision Making: Resection vs Ablation

AI recommended treatment strategy shows better survival

患者ごとに最も高い生存率になる
AIが推定した治療法

肝癌の治療法判別AIの予測結果検証
イメージ

テストデータ

インプット

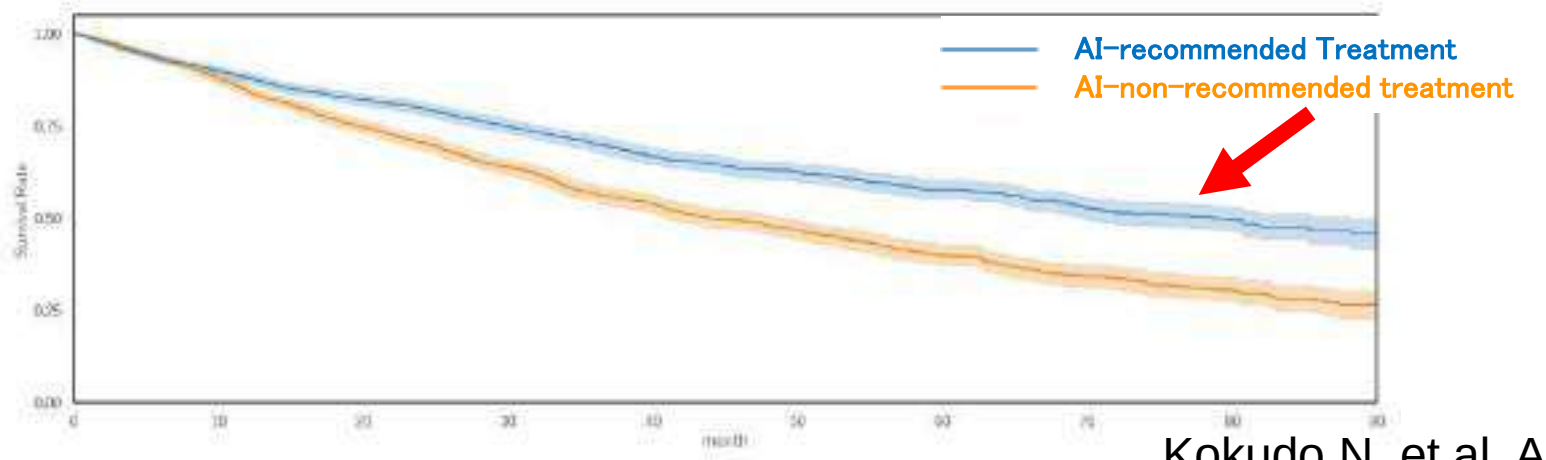
ID	治療方法	年齢	性別	体重	PS	…
1	肝切除	74	男性	58.6	1	
2	肝切除	66	女性	45	0	
3	ラジオ波焼灼	83	男性	100	1	

訓練済みAI

アウトプット

ID	推奨治療	実際の治療方法との一致
1	肝切除	Yes
2	ラジオ波焼灼	No
3	ラジオ波焼灼	Yes

OS K-M curve: AI-recommended vs non-recommended Treatment



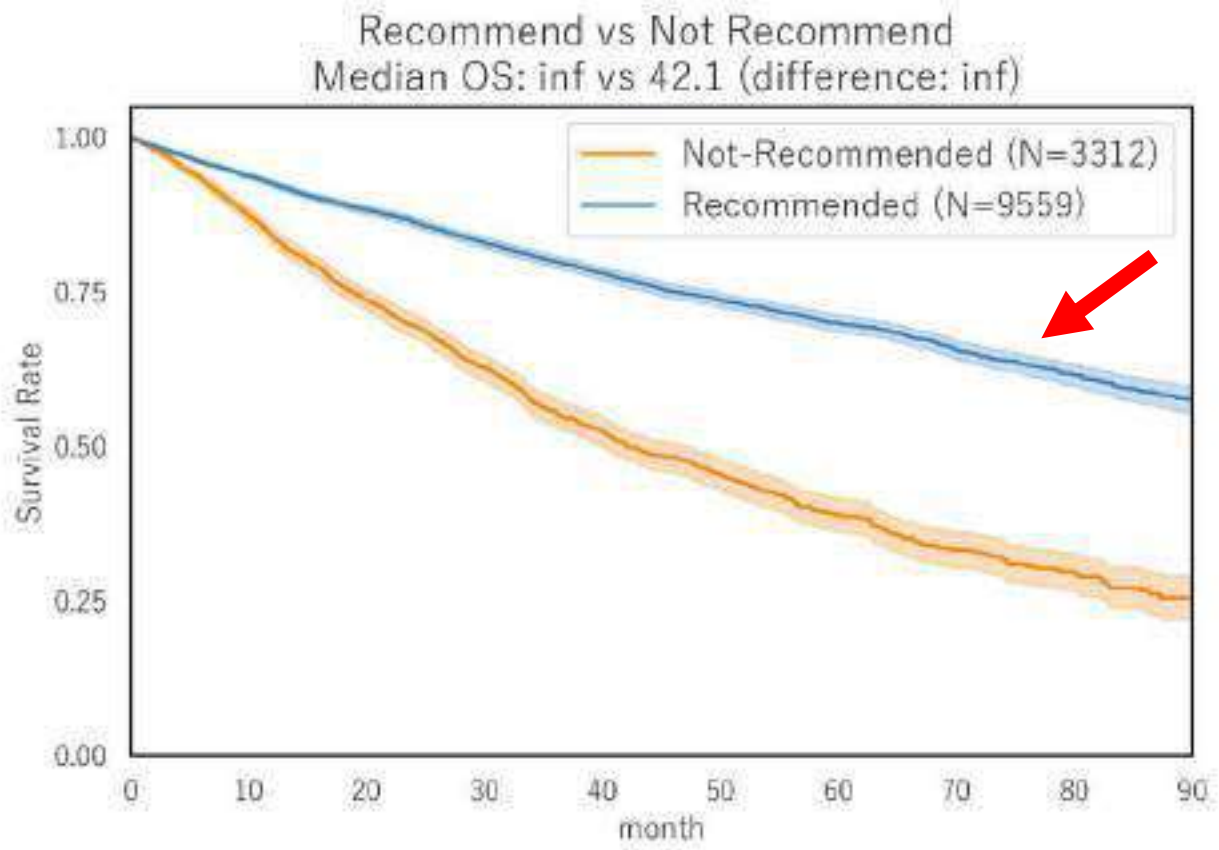
Kokudo N, et al. AI hospital Project 2024

AI-based Treatment Decision Making: Resection vs TACE

Results

テスト条件	データ件数	訓練データ(平均):11584 テストデータ(平均):1287
テスト結果	C-index	**0.73**
	Median OS	**差分: NA** Recommend: NA Not recommend: 42.1

Treatment	Actual number	AI-recommend
Resection	9587	**12325**
TACE	3284	546



AI recommended treatment strategy shows **better survival**

Kokudo N, et al. AI hospital Project 2024

Conclusion

- The surveillance of HCC high-risk patients detect many small curable HCC, leading to receiving potentially curative therapy (Resection, Ablation, transplantation), providing patients a very long survival.
- This also saves the medical cost for advanced stage HCC, such as expensive immunotherapy/molecular targeted therapy.
- Academic society should corroborate both with patients' advocacy and Government to implement this system.

Thank you very much for your kind attention.

Kindai University, Japan

Coffee Break

APAC Hepatocellular Carcinoma Policy Forum 2024

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

APAC Hepatocellular Carcinoma Policy Forum 2024

Bangkok October 2, 2024

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

厚生労働省 ひと、くらし、みらいのために Ministry of Health, Labour and Welfare

2024
Hepatocellular Carcinoma (HCC)
APAC Policy Forum

Bangkok, Thailand

2 October 2024

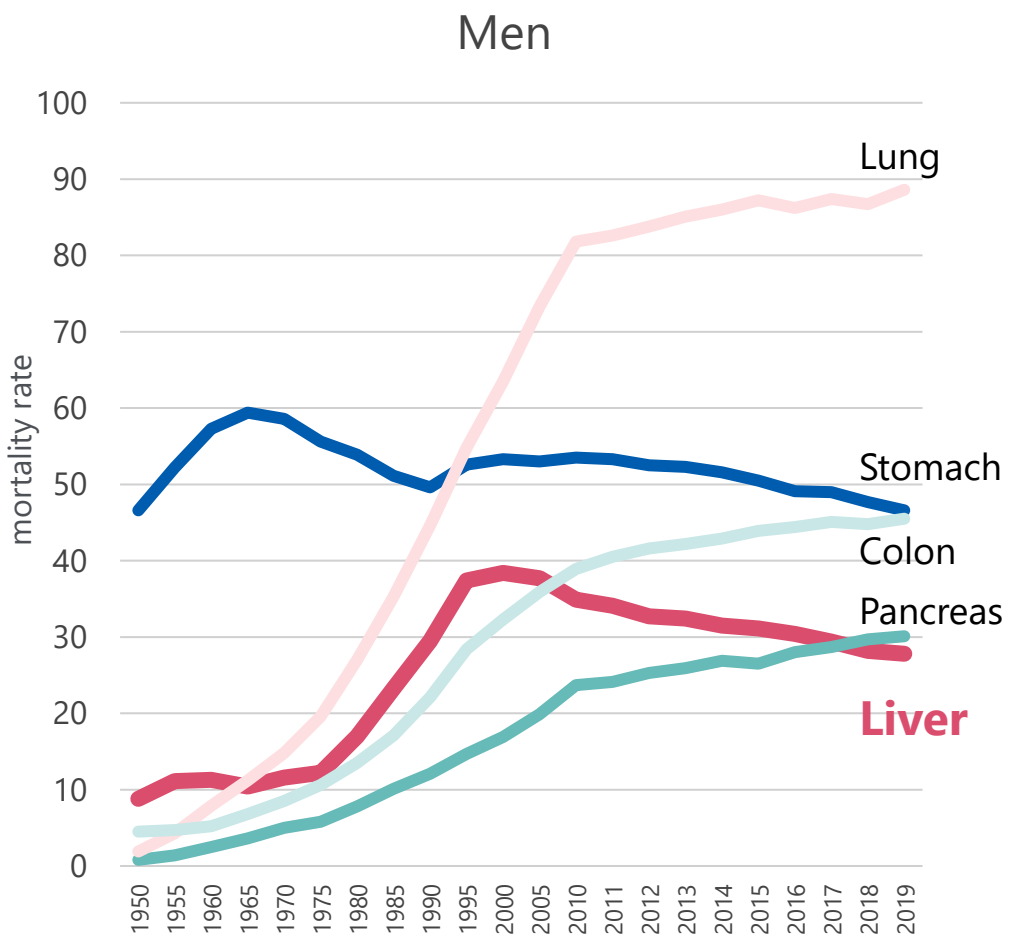
Measures against Liver Diseases in Japan

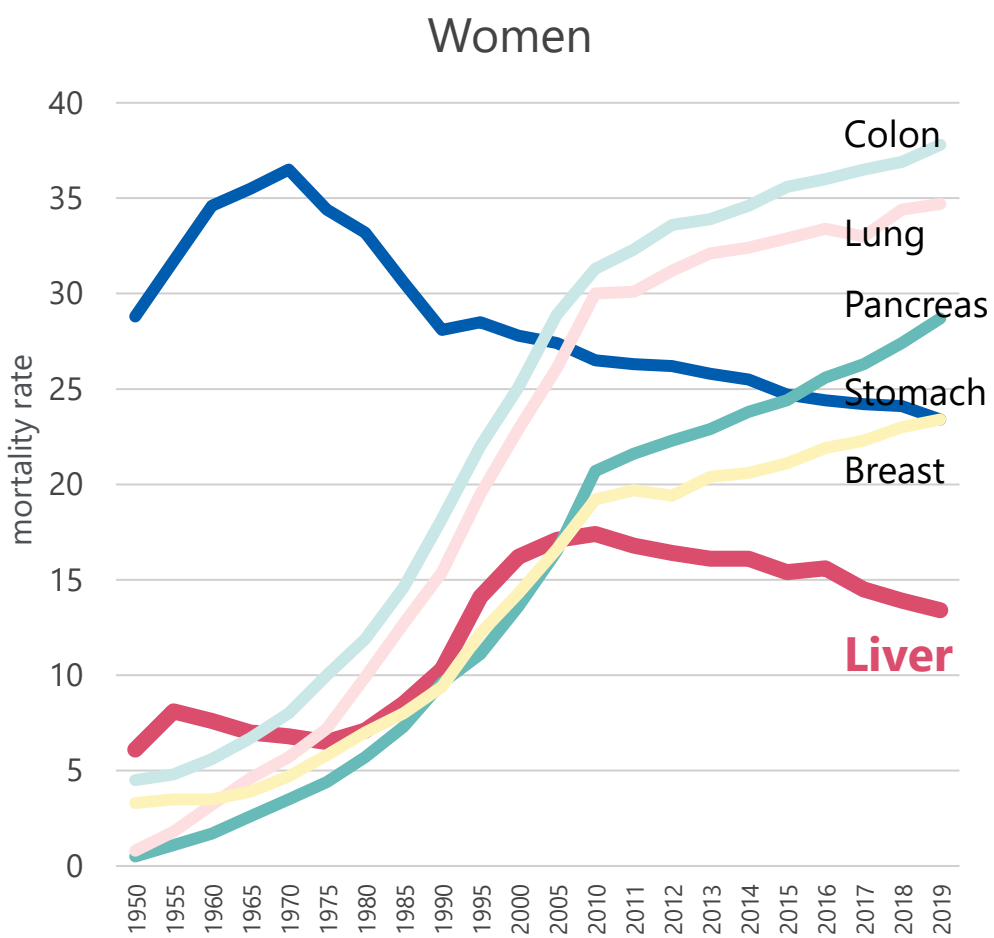
Dr. Kiyono Sōichirō, MD, PhD 清野 宗一郎

Assistant Director,
Hepatitis Control and Prevention Office

Ministry of Health, Labour and Welfare of Japan

Mortality Rate due to Cancers in Japan



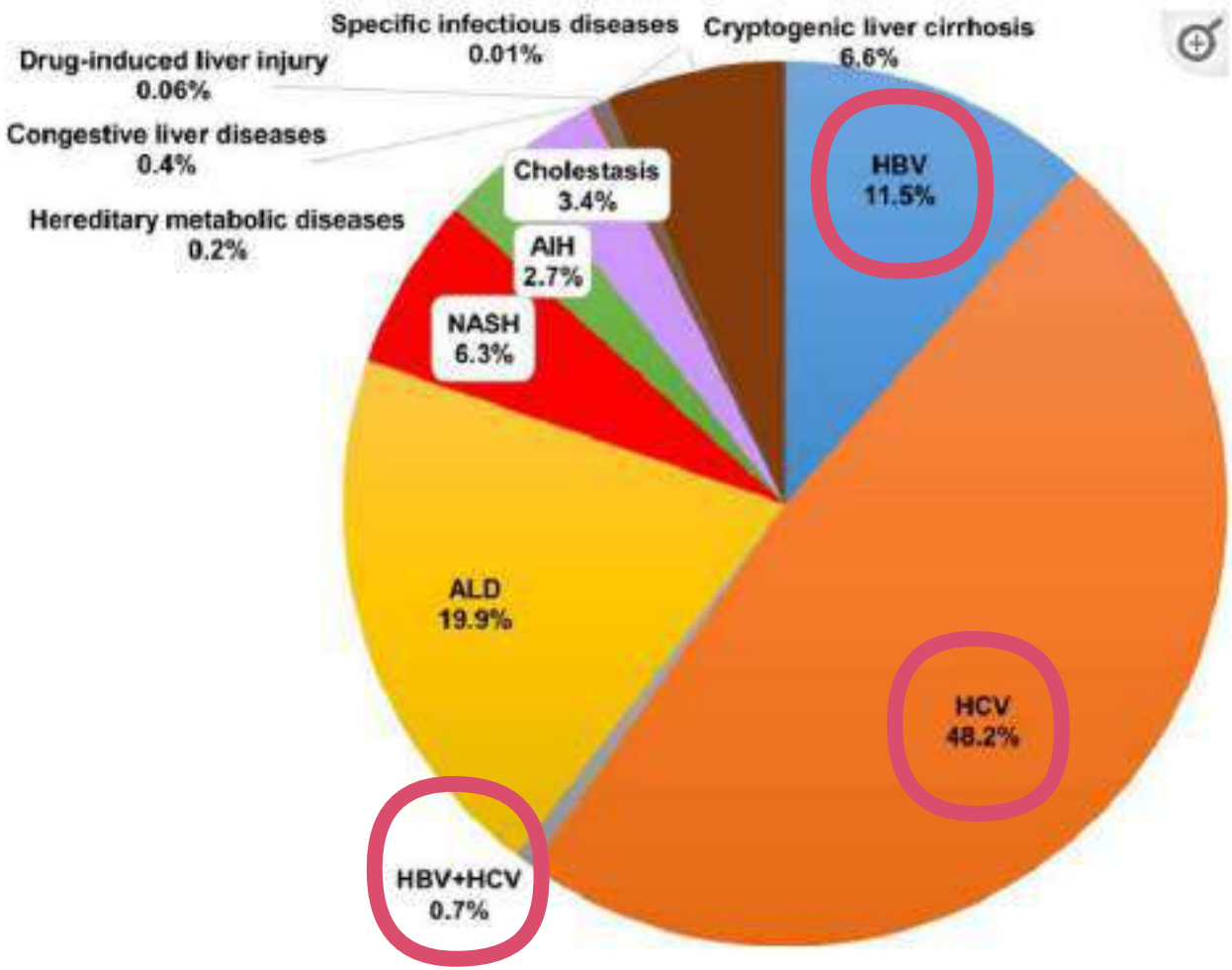


The mortality rates of liver cancers are decreasing in recent years in Japan.

Compiled by the author. Data from Vital Statistics of Japan: https://www.e-stat.go.jp/stat-search/files?page=1&toukei=00450011&tstat=000001028897 .

Cause of Cirrhosis in Japan

N = 48,621



Over 60 % of the patients with cirrhosis are caused HBV or HCV infection.

Enomoto H, et al. J Gastroenterol. 2020

History of Hepatitis Measures

1985	**Prevention project** of mother-to-child transmission of hepatitis B began.
2006	Hepatitis B lawsuit: Supreme Court decision was made. Hepatitis C lawsuit: High Court in Osaka recommended settlement.
	Hepatitis virus infection became a social issue.
2008	**Comprehensive measures** against hepatitis started. "Law on Special Measures against Hepatitis C" came into effect (for the infected persons by such as fibrinogen products).
2010	**"Basic Law on Hepatitis Measures"** went into effect.
2012	"Law on Special Measures against Hepatitis B" came into effect (for the infected persons through mass vaccination).
2016	Hepatitis B vaccine was placed on the routine immunization list under the Immunization Law.
2018	Public funding of medical expenses of the treatment of hepatic cancer and severe cirrhosis started under the research promotion project.

Prevention of Mother-to-Child Transmission

1985

Projects below was implemented by local governments, with half of national government subsidy.

for pregnant women: HBs antigen test

for HBs-antigen-positive pregnant women: HBe antigen test

to children of an HBs-antigen and HBe-antigen-positive pregnant woman:
2 doses of HB immunoglobulin (HBIG) and 3 doses of HB vaccine

HBV carrier rate

Before start of project
0.26% → 0.024%
9 year after

9-year-olds born in 1978
0.98% → 0.03—0.06%
School children born between 1985—1989
in Iwate

10- or 11-year-olds born before 1985
0.3% → 0.03%
School children after start of project
in Shizuoka

1995 The HBIG and HB vaccines covered by health insurance.

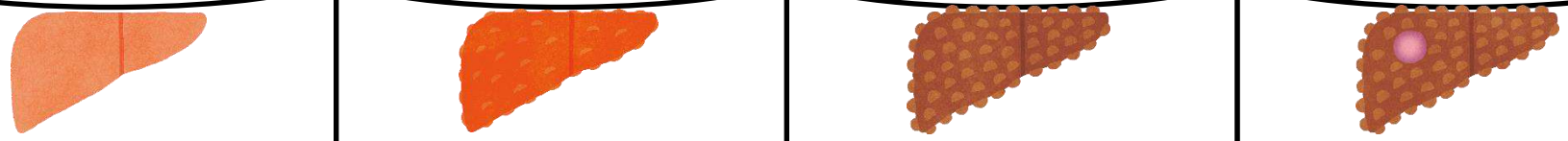
2016 HB vaccine was designated as one of routine vaccination for all the newborns.

Hepatitis Progression and Countermeasures

Infection

10 to 40 years

Asymptomatic | **Chronic hepatitis** | **Cirrhosis** | **Hepatic cancer**



Hepatitis virus test

Serious illness prevention measures

If the test is positive, **First full examination**

When follow-up is required, **Periodic inspection**

Medical expenses subsidy for hepatitis

- Interferon therapy
- Nucleic acid analog therapy
- Interferon-free therapy

10,000 – 20,000 JPY per month

Treatment and research promotion project for hepatic cancer and severe cirrhosis

Inpatient care

10,000 JPY depending on the income

Outpatient treatment for hepatic cancer

National Budget for Hepatitis Measures in Japan

1,000 JPY = 7 USD (as of 2 Sept 2024)

	Total in FY 2024	*Approx. 16,800,000,000 JPY*
1	Promoting hepatic disease treatment	Approx. 8,400,000,000 JPY
2	Promoting hepatitis virus test and severe illness prevention	Approx. 3,900,000,000 JPY
3	Strengthening local systems of the treatment	Approx. 500,000,000 JPY
4	Spreading correct knowledge to the public	Approx. 200,000,000 JPY
5	Promoting of research	Approx. 3,800,000,000 JPY

Basic Law on Hepatitis Measures enacted in 2010

What is described

- Basic philosophy
- Responsibilities of the national government, local governments, medical insurers, citizens, and physicians
- Establishment of guidelines for promotion of hepatitis measures
- Basis of hepatitis measures

Basic measures

Promoting

- Prevention and early detection
- Equalization of hepatitis medical care
- Research

Respect for human rights of hepatitis patients and elimination of discrimination

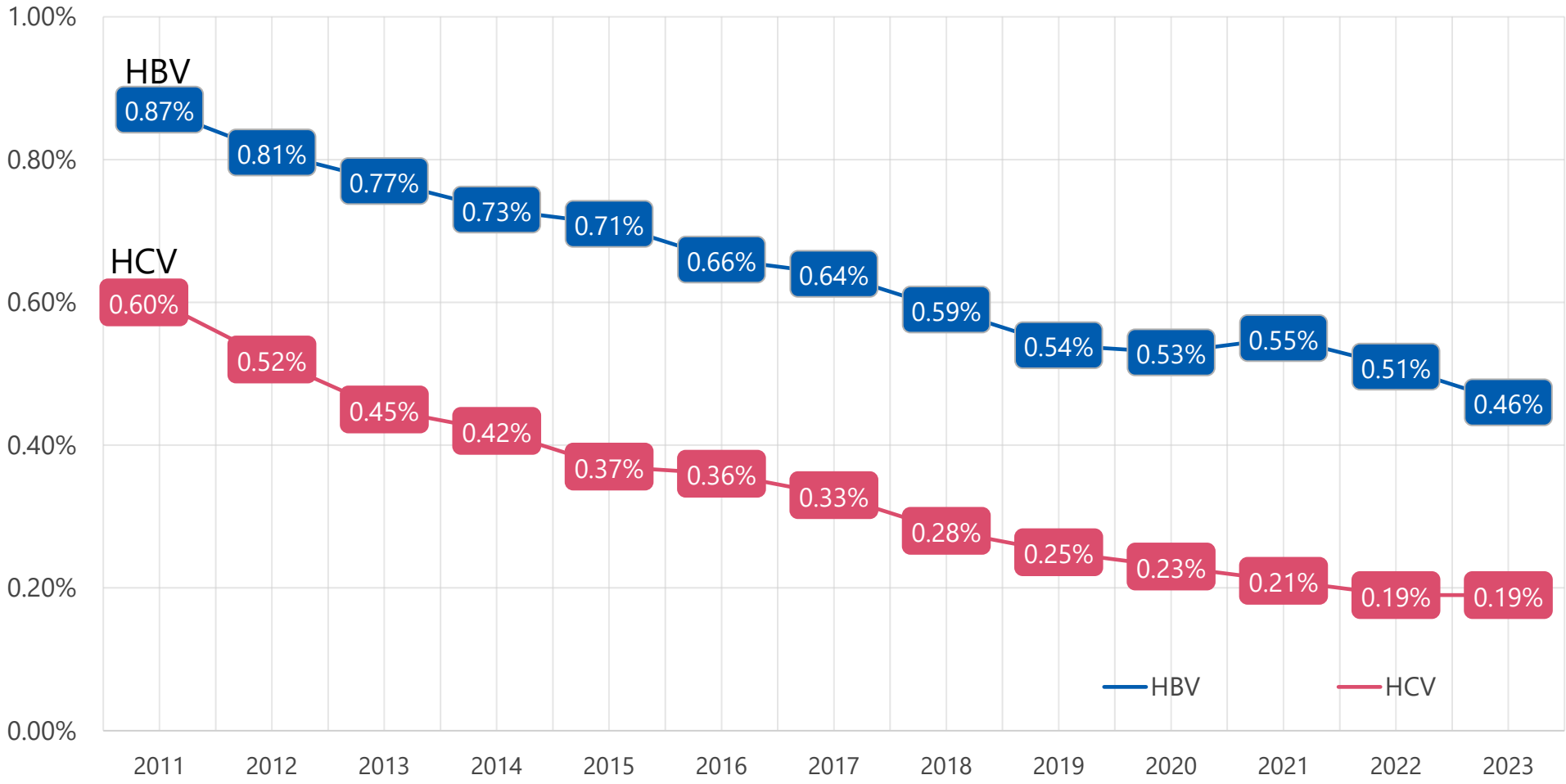
Formulation of basic guidelines

History Related to Hepatitis Testing in Japan

2002	Milestone checkups by local governments implemented. (Notice are made for citizens at 40, 45, 50, … years old.)
	Testing at public health centers installed.
2007	Testing sites expanded to medical institutions.
2008	Comprehensive measures against hepatitis started.
2011	“Basic Law on Hepatitis Measures” enacted.
	Hepatitis awareness raising campaign “Shitte Kan’en (Let’s learn about hepatitis)” launched.
2014	The cost of initial and periodic inspections were subsidized.
	Testing for citizens at 40 years old and older in health promotion projects subsidized.
2017	Testing-at-your-workplace promotion project began.
2018	Easy-to-find-your-nearby-testing-place websites launched.

Hepatitis Virus Test Positivity Rates in Japan

Tests provided by local governments

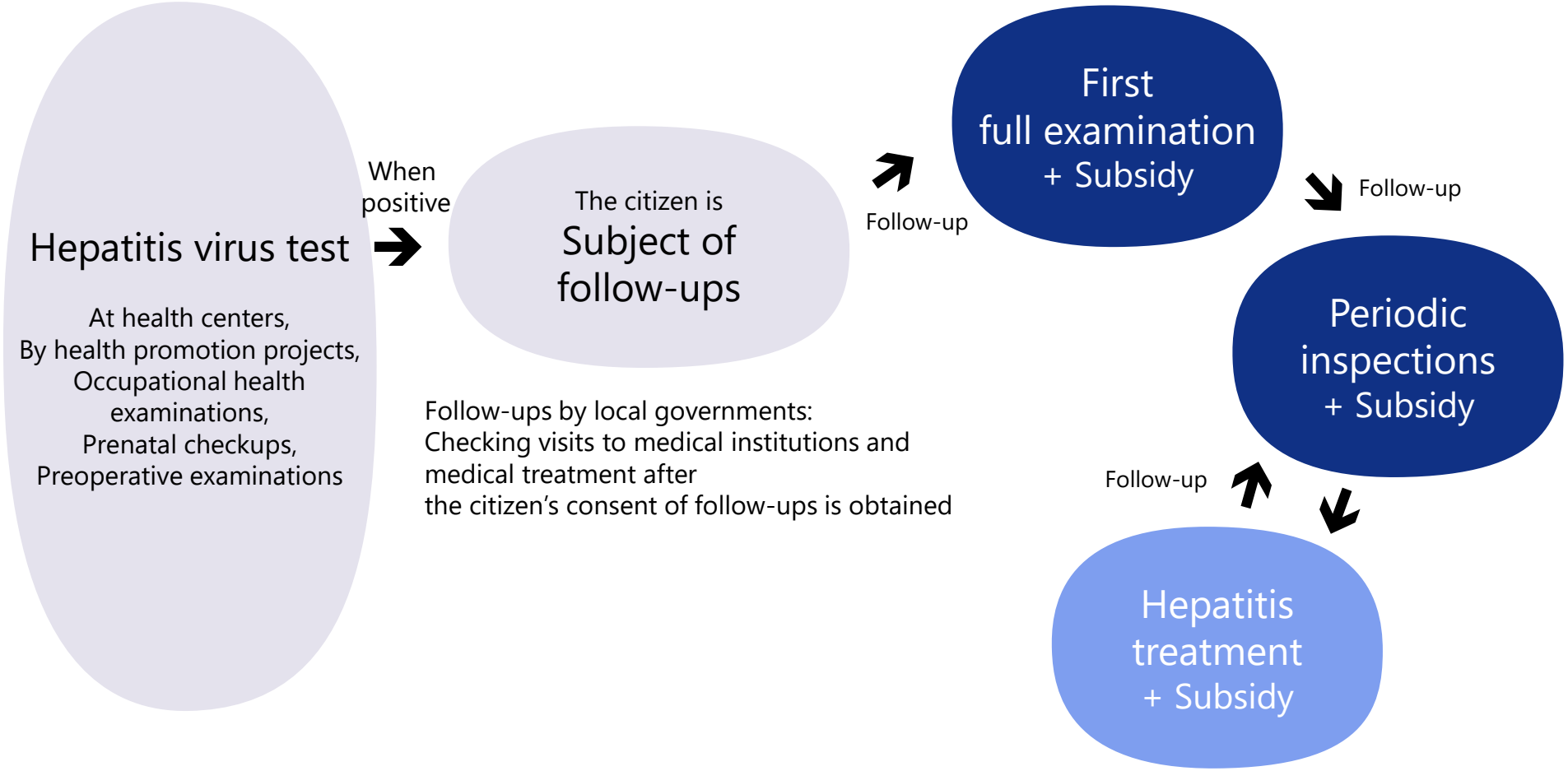


The rates of HBV/HCV-positive are decreasing in Japan.

Serious Illness Prevention Project for Test-Positive Patients

Serious illness prevention project includes:

Early detection of hepatitis virus-positive persons
Early treatment of positive persons through consultation and follow-ups
Prevention of serious illness in patients with viral hepatitis



Hepatitis Medical Expense Subsidies

Special promotion program for hepatitis treatment

Implementator: Local governments
Financial support: Nation 1/2; Local governments 1/2

Target	Patients with hepatitis B or C virus infection
Covering medical cares	Chronic hepatitis B: **Interferon therapy, Nucleic acid analog therapy** Chronic hepatitis C, Liver cirrhosis C: **Interferon therapy, Interferon-free therapy**
Patient's own expenses	Up to 10,000 JPY per month (20,000 JPY for upper income patients)

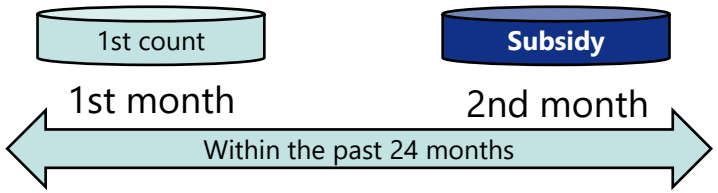
The subsidy coverage for medical cares has been increased year by year.

Subsidy for Patients with Severe Hepatic Diseases

"Project to Promote Research on the Treatment of Hepatic Cancer and Severe Cirrhosis" includes:

Reducing the burden of medical costs on patients
Promoting research on treatment of hepatic cancer and severe liver cirrhosis
Collecting clinical data
Developing medical guidelines

Subjects for subsidies	Patients	with hepatic cancer or severe cirrhosis caused by hepatitis B or C virus
	Annual income	Approx. 3.7 million JPY or less
Subsidy details	Inpatient care	Treatment for hepatic cancer or severe cirrhosis
	Outpatient care	Molecular targeted drugs Immune checkpoint inhibitors Liver chemotherapy Particle radiation therapy
Copayment	10,000 JPY per month	



The subsidy starts from the 2nd month
in which the maximum amount of high medical care cost is exceeded.

Role of Core Hospitals for Liver Diseases

One or more hospitals in a prefecture are designated as “core hospitals for liver diseases.”

- Providing information on liver diseases
- Collecting and providing information on medical institutions specialized for liver diseases
- Organizing training sessions and lectures for healthcare professionals
- Consulting and supporting for liver diseases
- Establishing forums with the medical institutions regarding liver diseases
- Generating medical systems that can provide multidisciplinary treatment for liver cancer

Hepatitis Medical Coordinators

Steps to combat hepatitis

Goals of the measures

Citizens

Step 0 **Prevention** → Step 1 **Test** → Step 2 **Seeing a doctor** → Step 3 **Treatment** →

Reducing the number of people who progress to cirrhosis and liver cancer

Hepatitis Medical Coordinators

coordinating the appropriate promotion of hepatitis cares utilizing their own strength


Public health nurses

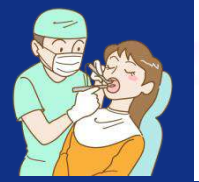

Patients


Local government officials


Office workers


Nurses


Physicians


Dentists


Clinical technologists


Pharmacists

Roles

Spreading understanding of hepatitis

Providing advice and information on hepatitis

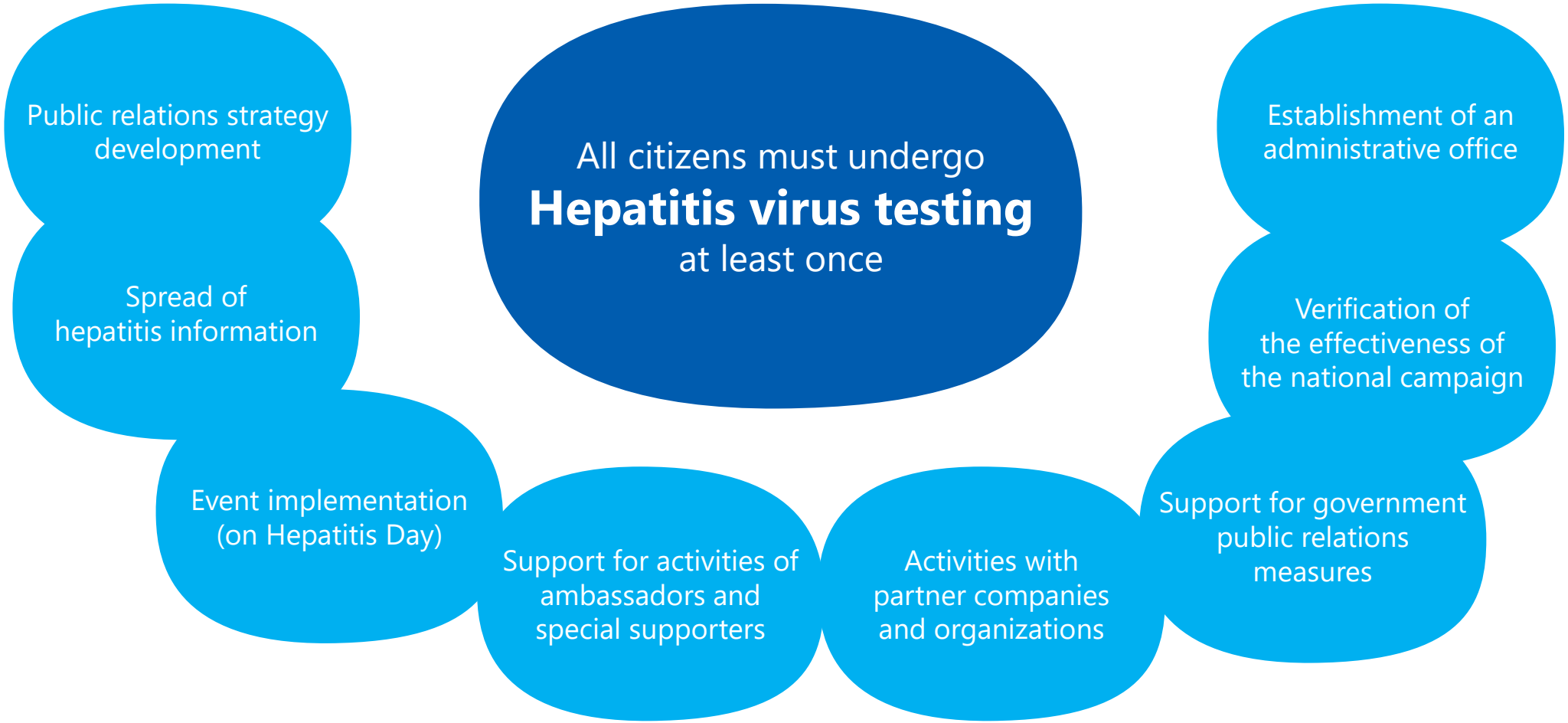
Encouraging people to take examinations

Explaining the support systems for hepatitis to the patients

Eliminating prejudice and discrimination against the patients

National Campaign to Raise Awareness of Hepatitis

To provide the public with correct knowledge on hepatitis
To encourage them to take action for early detection and early treatment



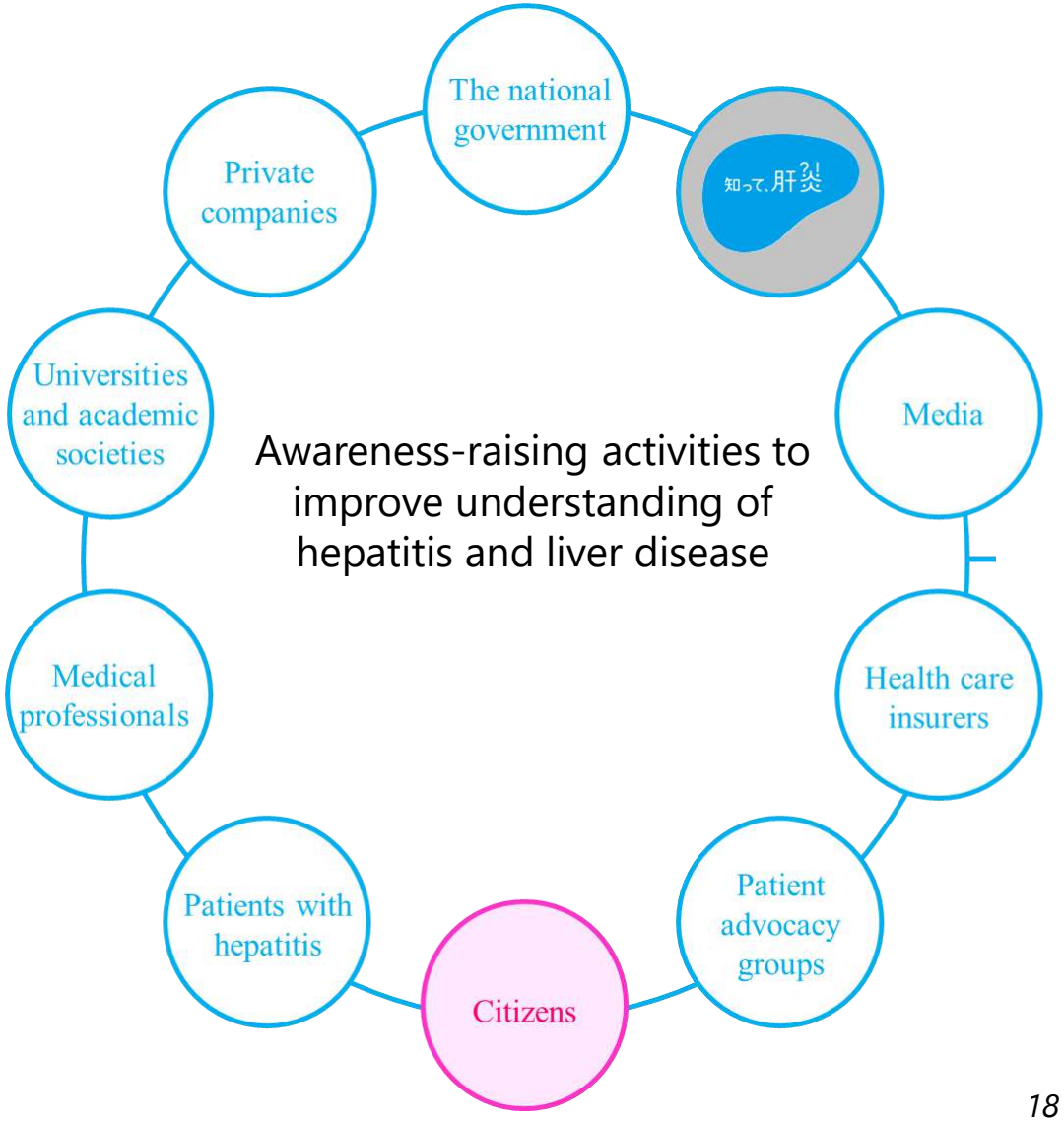
Through a wide variety of media and in collaboration with private companies

Spreading Accurate Information of Hepatitis to the Public

Shitte Kan'en (Let's Learn about Hepatitis) campaign

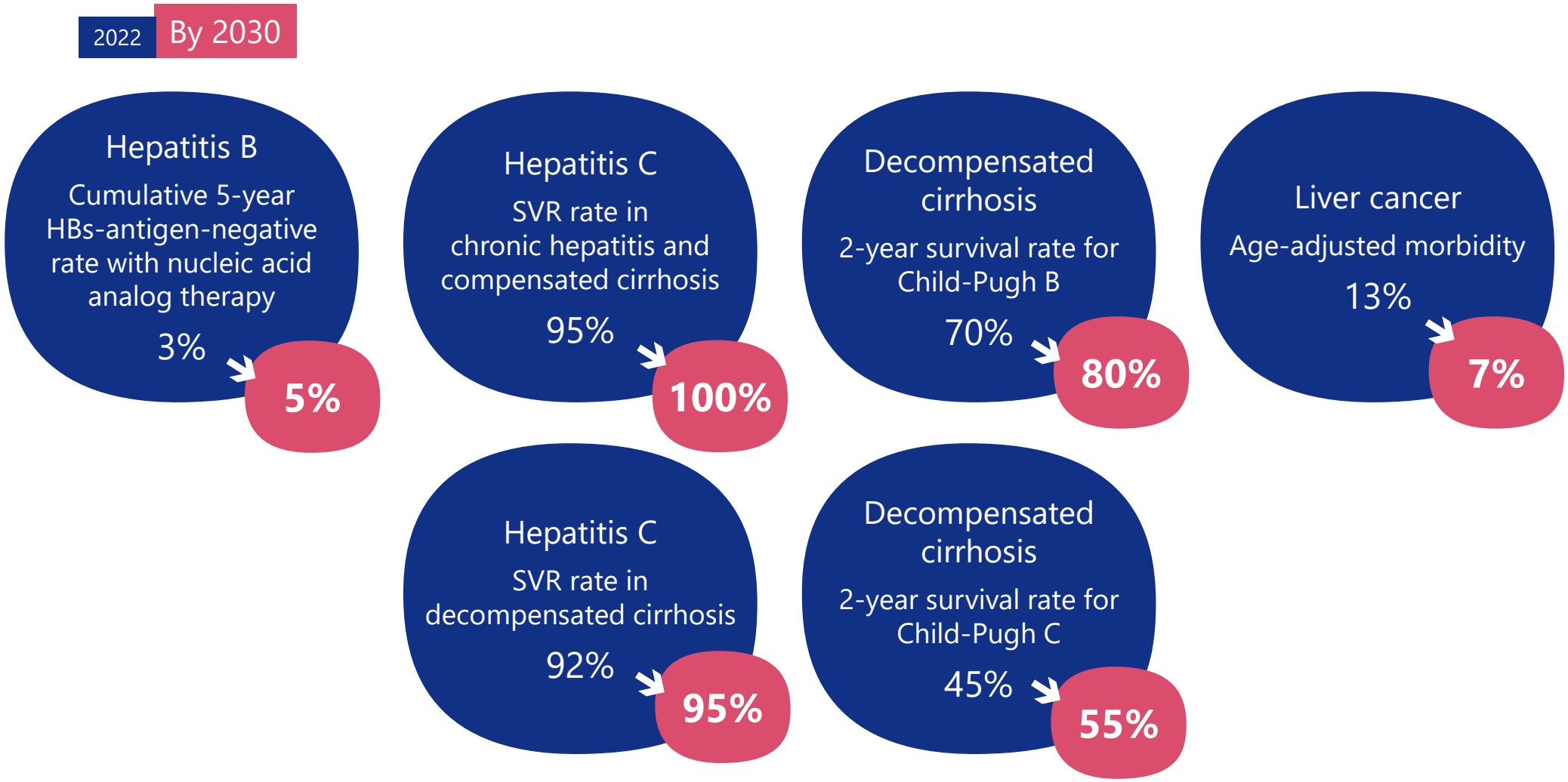
Hepatitis: Think Again

Events are held all over in Japan by popular performers.



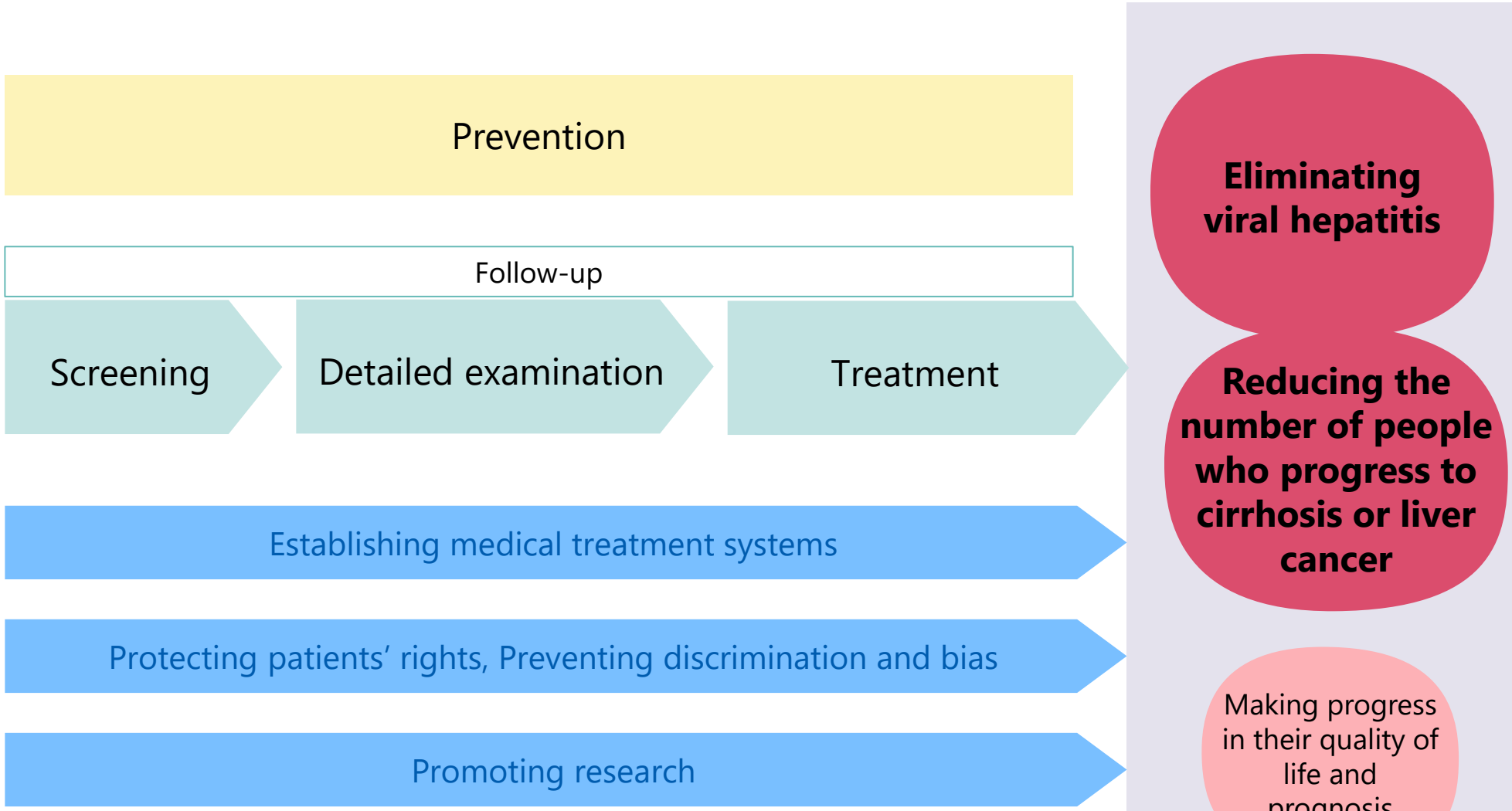
Hepatitis Research Promotion Strategy

Established to address need for further promotion of research.



SVR: Sustained virological response, which means hepatitis C virus is not detected in your blood.

Summary


Prevention
Follow-up
Screening
Detailed examination
Treatment
Establishing medical treatment systems
Protecting patients' rights, Preventing discrimination and bias
Promoting research
Eliminating viral hepatitis
Reducing the number of people who progress to cirrhosis or liver cancer
Making progress in their quality of life and prognosis

What we have done so far…

- Surveying and assessing the status of viral hepatitis and the liver diseases in our country
- Establishing and strengthening surveillance systems for viral hepatitis
- Developing viral hepatitis prevention,
  Preventing mother-to-child transmission of hepatitis B
- Strengthening treatment system for viral hepatitis and liver diseases
- Spreading accurate knowledge to citizens
- Protecting patients' rights

APAC Hepatocellular Carcinoma Policy Forum 2024

Bangkok October 2, 2024

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

APAC Hepatocellular Carcinoma Policy Forum 2024

Bangkok October 2, 2024

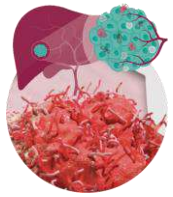
Optimizing HCC Surveillance in Thailand

Clinical and Economic Benefits of Using New Biomarker

PROF. PISIT TANGKIJVANICH

Faculty of Medicine,
Chulalongkorn University,
Bangkok, Thailand

OUTline of the PRESENTATION



Optimizing HCC surveillance in Thailand
Clinical and Economic Perspectives

- √ Status of HCC surveillance in Thailand
- √ Conventional and emerging tools for HCC surveillance
- √ HECON study using GAAD for HCC surveillance
- √ Summary and Perspective

QA

1

Current Status

Epidemiology

HEPATOCELLULAR CARCINOMA in THAILAND

Current Situation
HCC in THAILAND

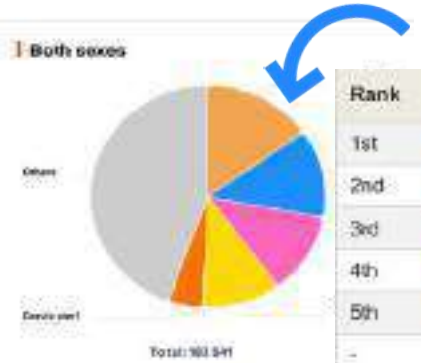
Statistics at a glance, 2022

GLOBAL CANCER OBSERVATORY

Number of new cases
183 541

Number of deaths
118 829

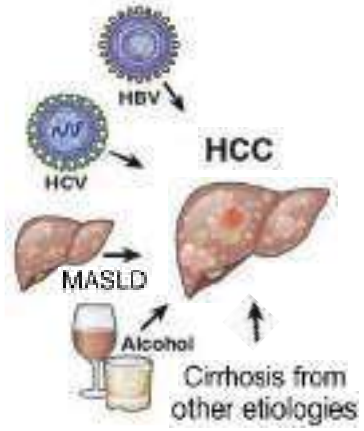
LIVER CANCERS **15.2%**



Rank	Cancer site	Number of cases	Percent
1st	Liver	27 936	15.2%
2nd	Lung	23 464	12.8%
3rd	Breast	21 628	11.8%
4th	Colorectum	20 173	11.0%
5th	Cervix uteri	8 662	4.7%
-	Others	81 648	44.5%

Number of new cases in 2022, both sexes, all ages

High-Risk Populations



Population group	Incidence of HCC
Sufficient risk to warrant surveillance	
Child-Pugh A–B cirrhosis, any etiology	≥ 1.0% per year
Hepatitis B	
Hepatitis C (viremic or post-SVR)	
Alcohol associated cirrhosis	
Nonalcoholic steatohepatitis	
Other etiologies	

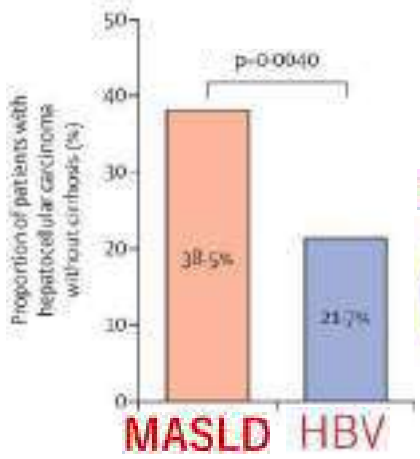
Cirrhosis

Metabolic Dysfunction-Associated Steatotic Liver Disease

MASLD
Metabolic Dysfunction Associated Steatotic Liver Disease

Metabolic Syndrome

T2DM



Non-CIRRHOSIS

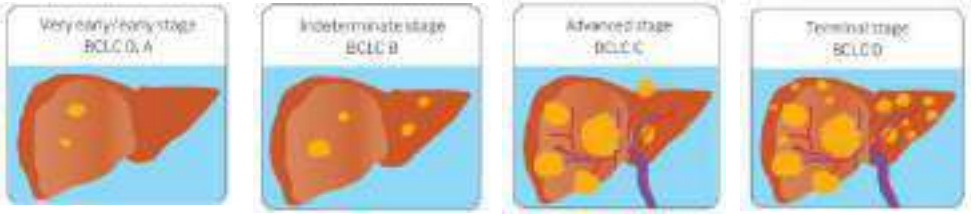
Tan DJH, et al. Lancet Oncol 2022

Current Treatment of HCC

CANCER STAGING

BCLC

Barcelona-Clinic Liver Cancer



Surgical treatment

Liver transplantation
Surgical resection
Local ablation

RFA

Locoregional treatment

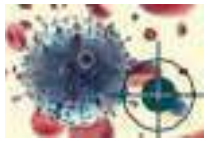
Transarterial chemoembolization

TACE

TransArterial RadioEmbolization

TARE

Systemic treatment



Best supportive care

HCC

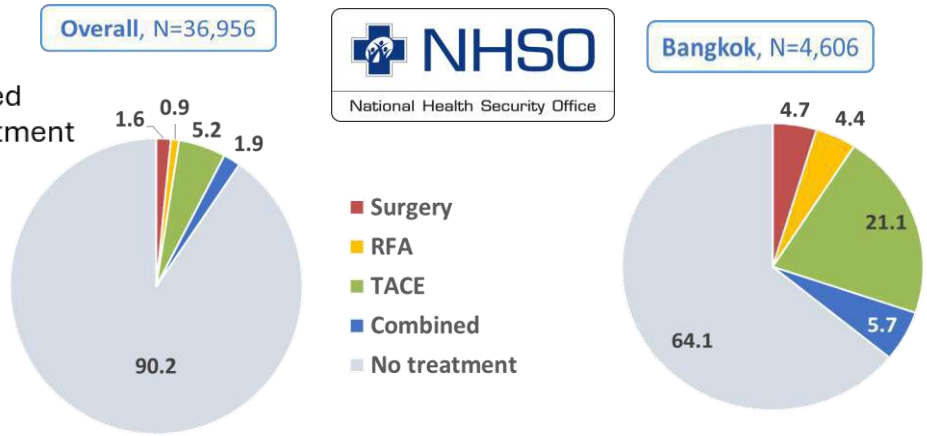
>60 months

Median Survival Time

3 months

Proportion of HCC undergoing different treatments in Thailand

2.5% received curative treatment



Kitiyakara T, et al. Asian Pac J Cancer Prev 2022

The surveillance program for HCC is not well implemented

Lack of EARLY DETECTION

In resource limitations

Several BARRIERS

Inadequate HCC AWARENESS & KNOWLEDGE

REIMBURSED POLICY

Surveillance tools

?

Surveillance

Hepatocellular Carcinoma

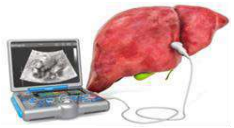
methods

Conventional and Emerging Tools for HCC Surveillance

International Guidelines

Current Recommendation

- HCC surveillance using **ultrasound (US) and alpha-fetoprotein (AFP) every 6 months is the standard of care** in high-risk populations, particularly cirrhosis



Data from Meta-analysis

- 32 studies (1990-2016, including 13367 patients) studied the sensitivity of US ± AFP for the detection of HCC in patients with cirrhosis

Conclusions: Using US + AFP increases the sensitivity of early HCC detection in clinical practice

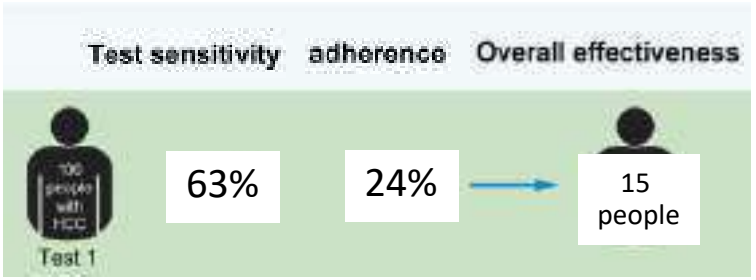
Tzartzeva K, et al. Gastroenterology 2018

Limitations of ultrasound-based screening

- Ultrasound has low sensitivity in early HCC, especially in obese patients with fatty liver
- Ultrasound is dependent on operator experience
- Ultrasound screening has poor adherence (e.g., barriers including the need for separate radiology appointments, costs, travel time)
- A meta-analysis showed rates of adherence of 24%

Wolf E, et al. Hepatology 2021

Low sensitivity in MASLD



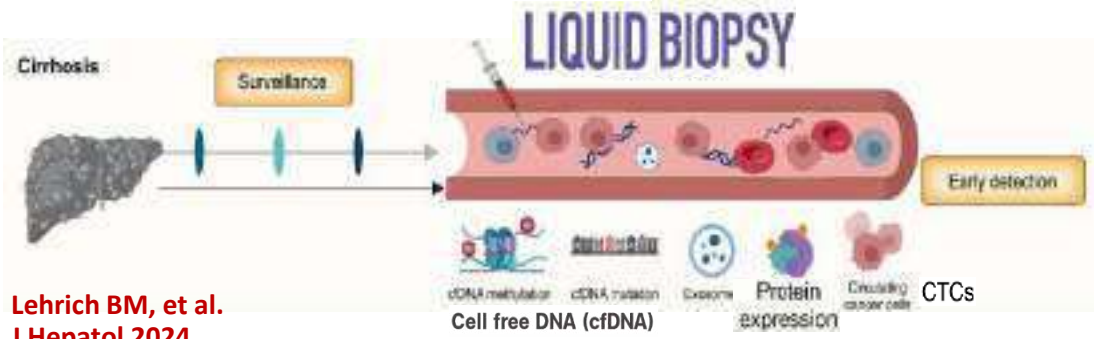
US + AFP ARE NOT ADEQUATE

Improving HCC surveillance

Moving beyond ultrasound-based screening ?

New Blood-based Biomarkers

Moving beyond ultrasound-based screening



Lehrich BM, et al.
J Hepatol 2024

NEW Tumor Markers

PIVKA-II (DCP)

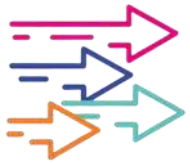
± AFP L3

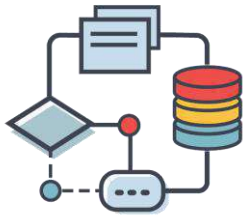
protein induced by vitamin K absence-II

des-gamma carboxy-prothrombin

+ AFP

Combination Assays





Algorithm

GALAD Score

Protein markers: AFP, AFP-L3, DCP; gender; age

GAAD score

gender age AFP DCP

Development and clinical validation of a novel algorithmic score (GAAD) for detecting HCC in prospective cohort studies

Teerha Piratvisuth[1] | Jinlin Hou[2] | Tawesak Tanwandee[3] |
Thomas Berg[4] | Arndt Vogel[5] | Jörg Trojan[6] | Enrico N. De Toni[7]
Masatoshi Kudo[8] | Anja Eiblmaier[9] | Hanns-Georg Klein[10] |
Johannes Kolja Hegel[11] | Kairat Madin[12] | Konstantin Kroeniger[12] |
Ashish Sharma[13] | Henry L.Y. Chan[14]

Hepatology Communications. 2023;7:e0317.

AFP

PIVKA-II (DCP)

DIGITAL

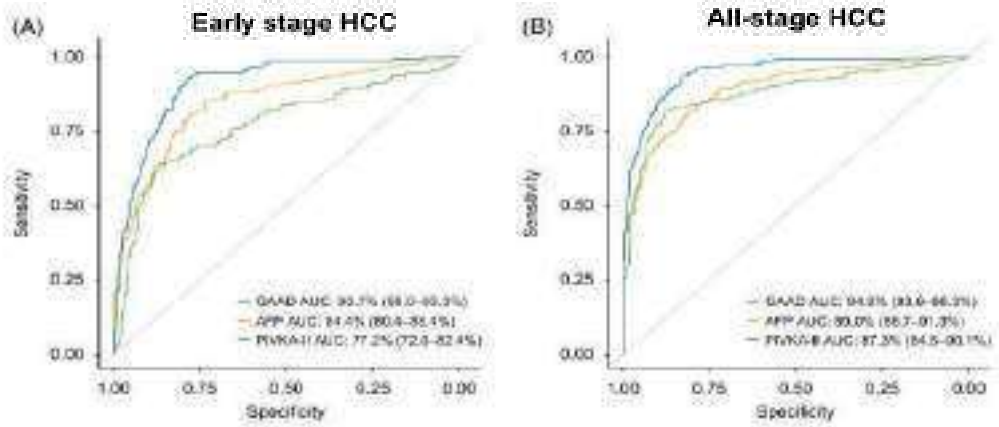
Algorithm

GAAD SCORE

GAAD = **G**ender, **A**ge, **A**FP, **D**CP (PIVKA-II)

Aid in diagnosis for **early-stage** HCC

GAAD cut-off score 2.57 (Range 0-10)



algorithm development ≈ validation study

AUC for differentiation between early-stage HCC and CLD was 91.4% with 70.1% sensitivity and 93.7% specificity.

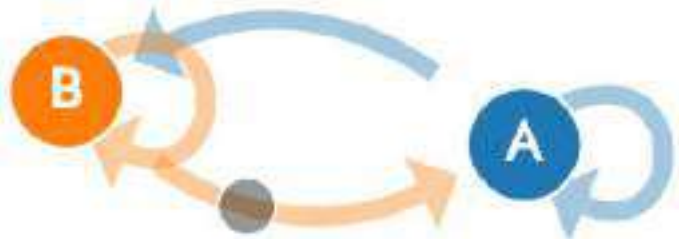
GAAD also showed strong specificity, with a lower rate of false positives regardless of disease stage, etiology, or region.

GAAD is better than AFP or PIVKA-II (DCP)

Conclusions: The GAAD algorithm significantly improves early-stage HCC detection for patients with CLD undergoing HCC surveillance.

Economic Model

MATHEMATICAL MODELING

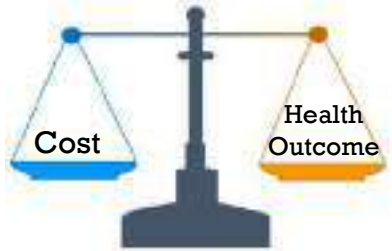


Cost–utility analysis (CUA)

Cost–utility analysis (CUA)

การวิเคราะห์ต้นทุนอรรถประโยชน์

- Defined as **the balance of costs and health outcomes** to determine whether an intervention justifies its cost.



- **Societal perspective (payers and patients)**
- Followed the Thai Health Technology Assessment (HTA) guidelines
- Estimated lifetime costs and health outcomes

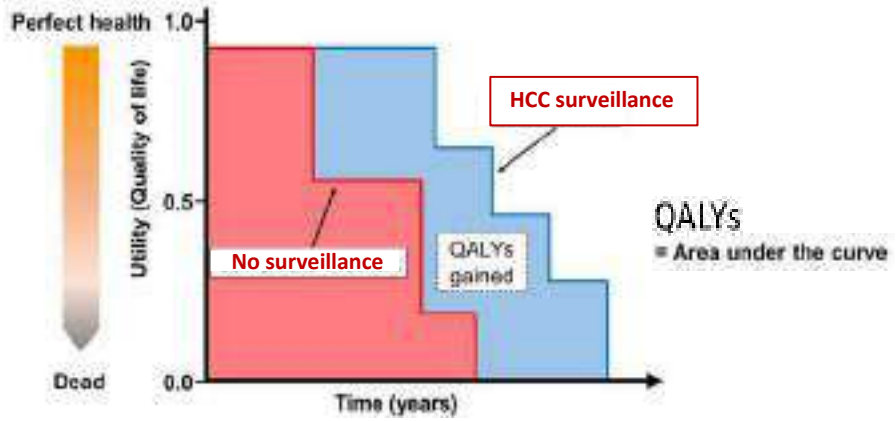
HEALTH Outcome

QALYs

quality-adjusted life years

ปีสุขภาวะ

A metric combining two-dimensional health outcomes:
- Quantity (length of life) and
- Quality of life (QOL)



Costs

Medical costs
(e.g., interventions, medication, hospitalization)
Non-medical costs
(e.g., travel for patients and caregivers)
Other costs

Incremental cost-effectiveness ratio (ICER)

$$ICER = \frac{(\text{Cost of A}) - (\text{Cost of B})}{(\text{QALY of A}) - (\text{QALY of B})}$$

อัตราส่วนระหว่างต้นทุนที่เพิ่มขึ้น เมื่อเทียบกับประสิทธิผลที่เพิ่มขึ้น

$$\text{Ratio} = \frac{\text{Cost}}{\text{Outcome}}$$

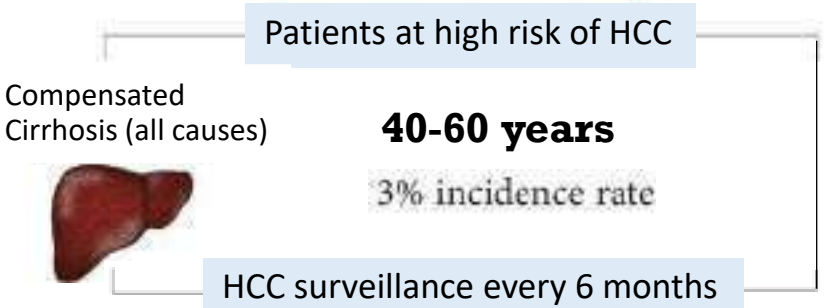
Willingness-to-pay (WTP) threshold

Thailand:
160,000 THB
=5000 USD

ความเต็มใจที่จะจ่าย

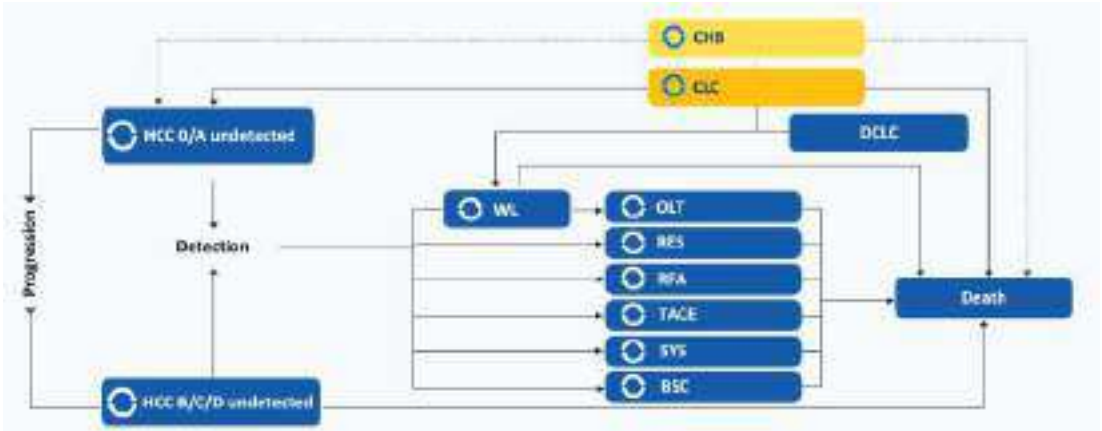
Target Population and Scope of the Model

PICO	Scenario
Population	Patients at high risk of HCC Compensated Cirrhosis (all causes) **40-60 years** 3% incidence rate
Intervention	HCC surveillance every 6 months
Comparison	No surveillance
Outcome	US US + AFP GAAD GALAD PIVKA-II + AFP



Markov model

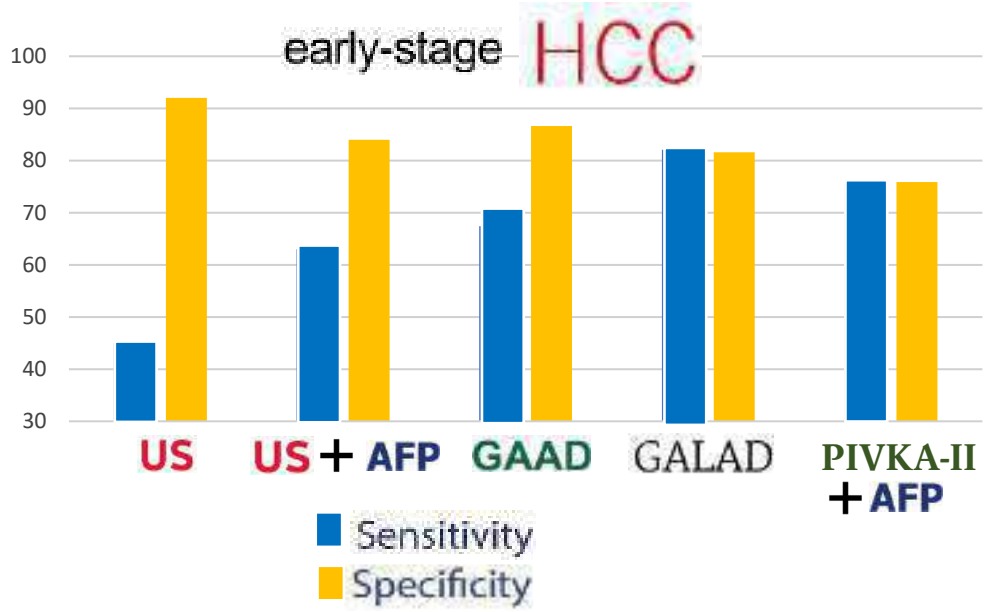
Microsimulation model reflecting the disease progression in cirrhosis



Data Input: Diagnostic Performance

Type of HCC surveillance

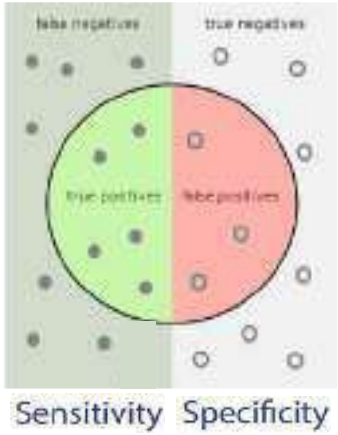
- 5 different screening methods plus 'no routine surveillance' were compared



Tzartzeva K, et al. Gastroenterology 2018;
Roche Diagnostics, Data on file;
Berhane S, et al. Clin Gastroenterol Hepatol 2016

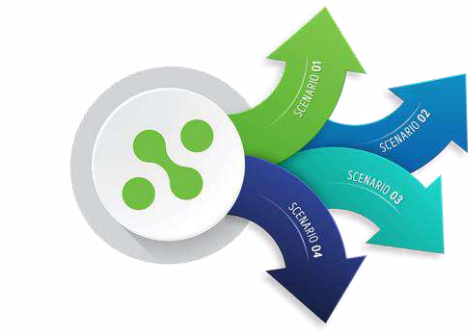
Sensitivity & Specificity

- **Higher sensitivity** is associated with a **higher early-detection** rate (higher true-positive rate) **and better survival**
- **Higher specificity** is associated with a **lower false-positive rate and lower unnecessary procedures & costs** (e.g., CT, MRI)



Sensitivity = True positive / True positive + false negative
True positive rate

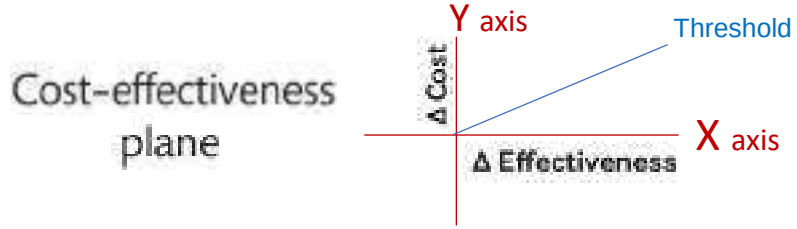
Specificity = True negative / True negative + false positive
True negative rate

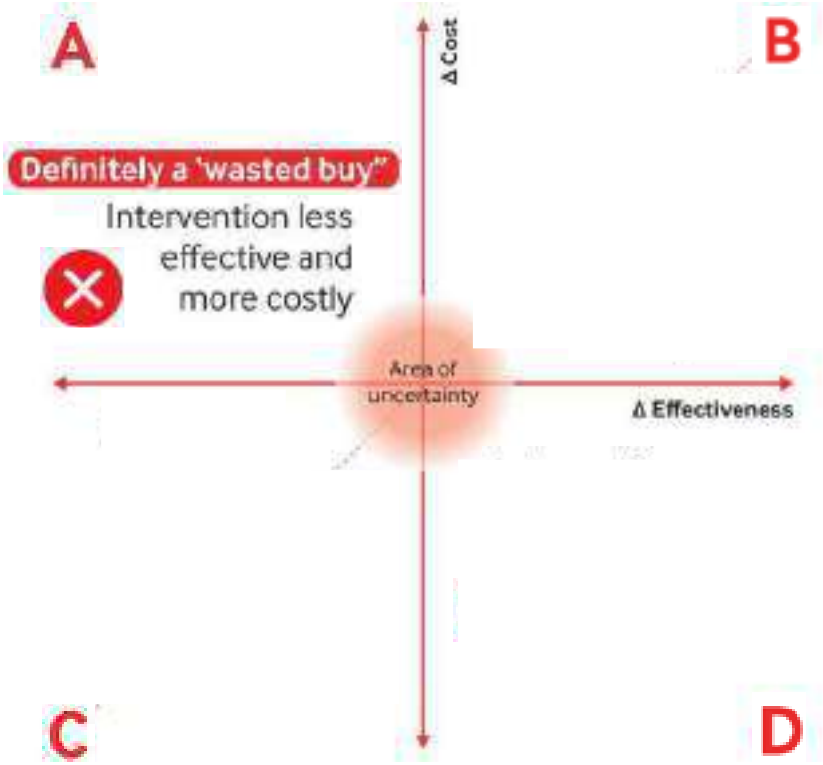


Base-case scenario 1:

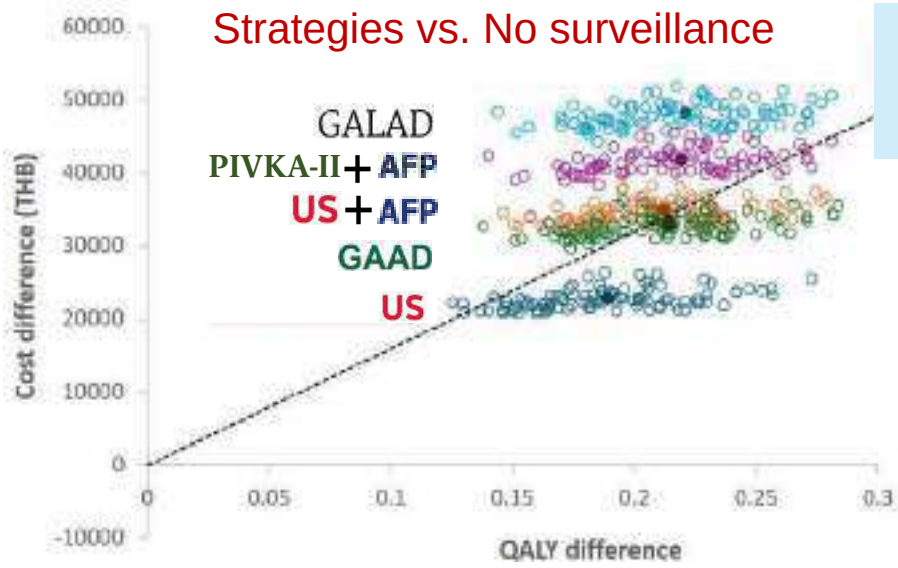
Surveillance strategies vs ‘No surveillance’ as the standard of care in compensated cirrhosis

Result Comparison for Surveillance Options





Strategies vs. No surveillance



Willingness-to-pay Threshold: THB 160,000/QALY

ความเต็มใจที่จะจ่าย

Base-case results

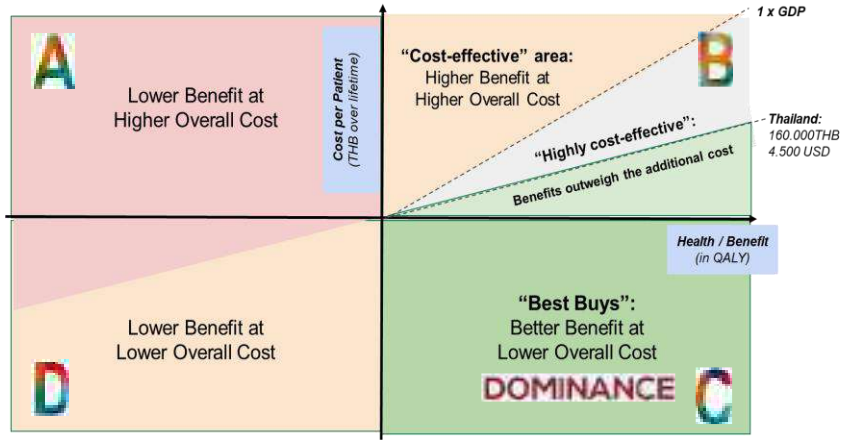
GALAD	ICER: THB218,529/QALY
PIVKA-II + AFP	ICER: THB191,388/QALY
US + AFP	ICER: THB164,943/QALY
Threshold	
GAAD	ICER: THB154,275/QALY
US	ICER: THB120,894/QALY

Ultrasound (alone) and **GAAD** appear to be cost-effective options in the base-case scenario

Base-case scenario 2:

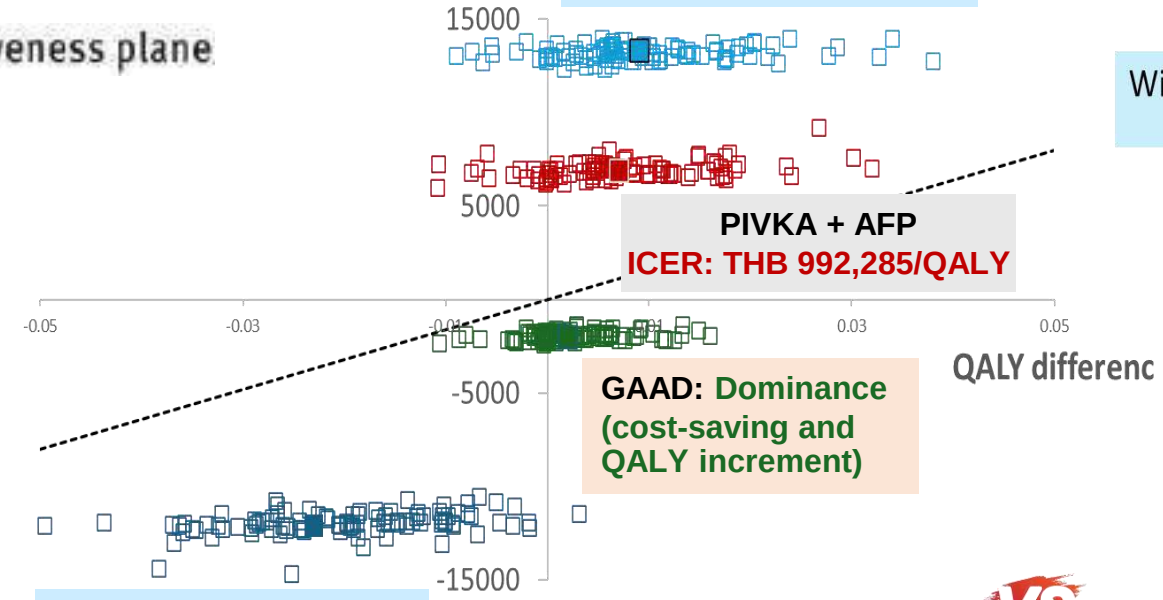
Surveillance strategies vs ‘US + AFP’ as the standard of care in compensated cirrhotis

Cost-effectiveness analysis by surveillance Strategies vs AFP+US as the standard of care



Cost effectiveness plane

GALAD
ICER: THB 1,480,777/QALY



Willingness-to-pay Threshold:
THB160,000/QALY

PIVKA + AFP
ICER: THB 992,285/QALY

GAAD: Dominance (cost-saving and QALY increment)

US alone: Loss of QALYs

VS

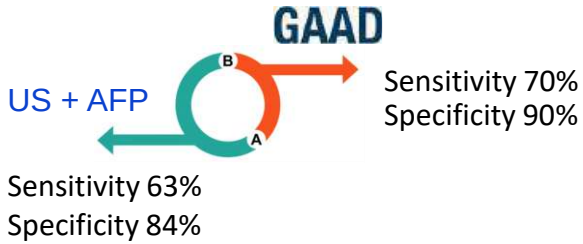
US + AFP

CONCLUSION

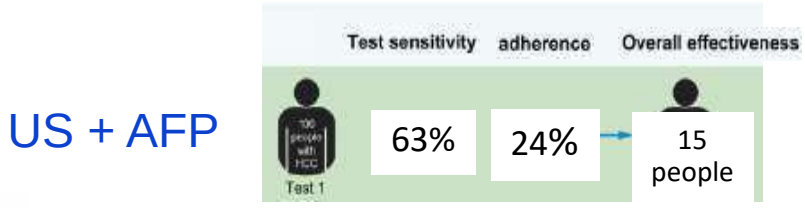
HCC surveillance in high-risk group esp., cirrhosis is significant regarding clinical and economic perspective

CLINICAL

GAAD VS US + AFP



GAAD has higher sensitivity for detecting early HCC and could have better adherence than US+AFP



one STOP SERVICES

GAAD

MORE Feasible option ⇨ Increasing Acceptance & UPTAKE

ECONOMIC

GAAD VS US + AFP

HEALTH ECONOMICS DATA

GAAD is suggested to be the dominant strategy (Cost-saving and QALY increment)

Future Perspectives

Implementation

GAAD is a suitable option for HCC surveillance in Thailand, considering its clinical and economic benefits, as well as the feasibility (one-stop service) and availability of the test

REIMBURSED POLICY HCC surveillance

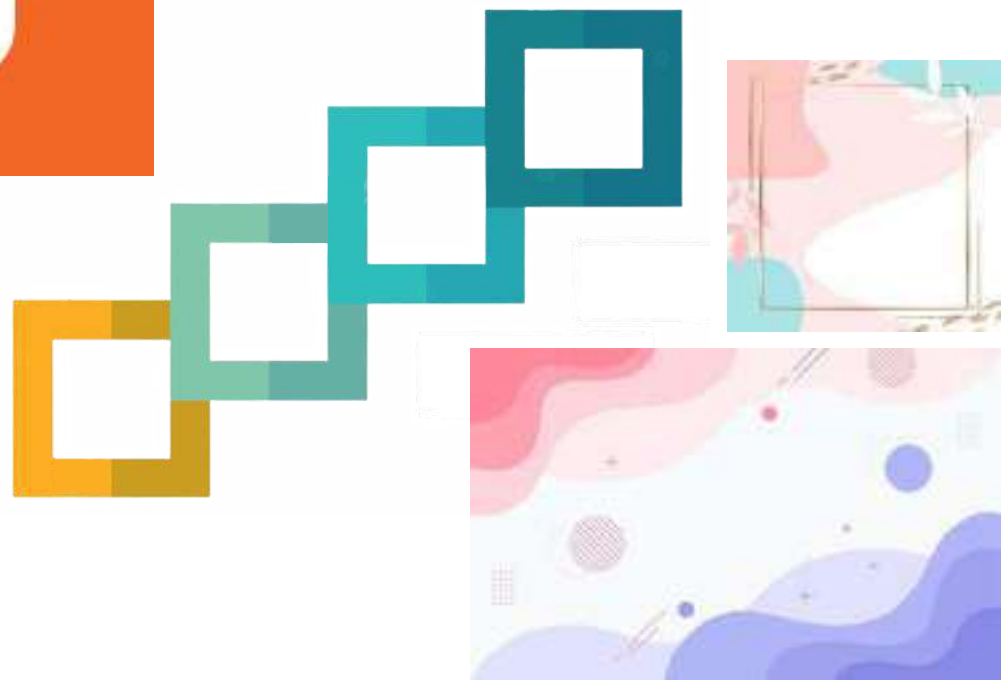
GAAD SCORE

CAPITATION → FEE-FOR-SERVICE

การเหมาจ่ายรายหัว

การจ่ายตามการให้บริการ

THANK YOU *for* YOUR ATTENTION



Coffee Break

APAC Hepatocellular Carcinoma Policy Forum 2024

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APAC Hepatocellular Carcinoma Policy Forum 2024

Bangkok October 2, 2024

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Panel 1

Progress report: HCC Surveillance and Management across APAC

Prof. Masatoshi Kudo (Moderator)
Professor & Chairman,
Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine
Japan

Ms. Do Thi Ngat
Officer, Medical Profession & Officer Health Protection Division
Department of Medical Service Administration, Ministry of Health
Vietnam

Dr. Murallitharan Munisamy
Managing Director
National Cancer Society Malaysia

Dr. Shi-Lun Wei
Deputy Director-General
Health Promotion Administration, Ministry of Health and Welfare
Taiwan

Prof. Simone Strasser
Head of Department & Senior Staff Specialist,
AW Morrow Gastroenterology and Liver Centre, Royal Prince Alfred Hospital
Australia

Dr. Somchai Thanasitthichai M.D.
Director
Thailand National Cancer Institute (NCI), Ministry of Public Health
Thailand

Prof. Dr. Teerha Piratvisuth
Chairman, Scientific Program,
Thai Association for the Study of the Liver
Thailand

Ms. Wen-Wen Yang Advisor and Lecturer
Taiwan Alliance of Patients' Organization
Taiwan

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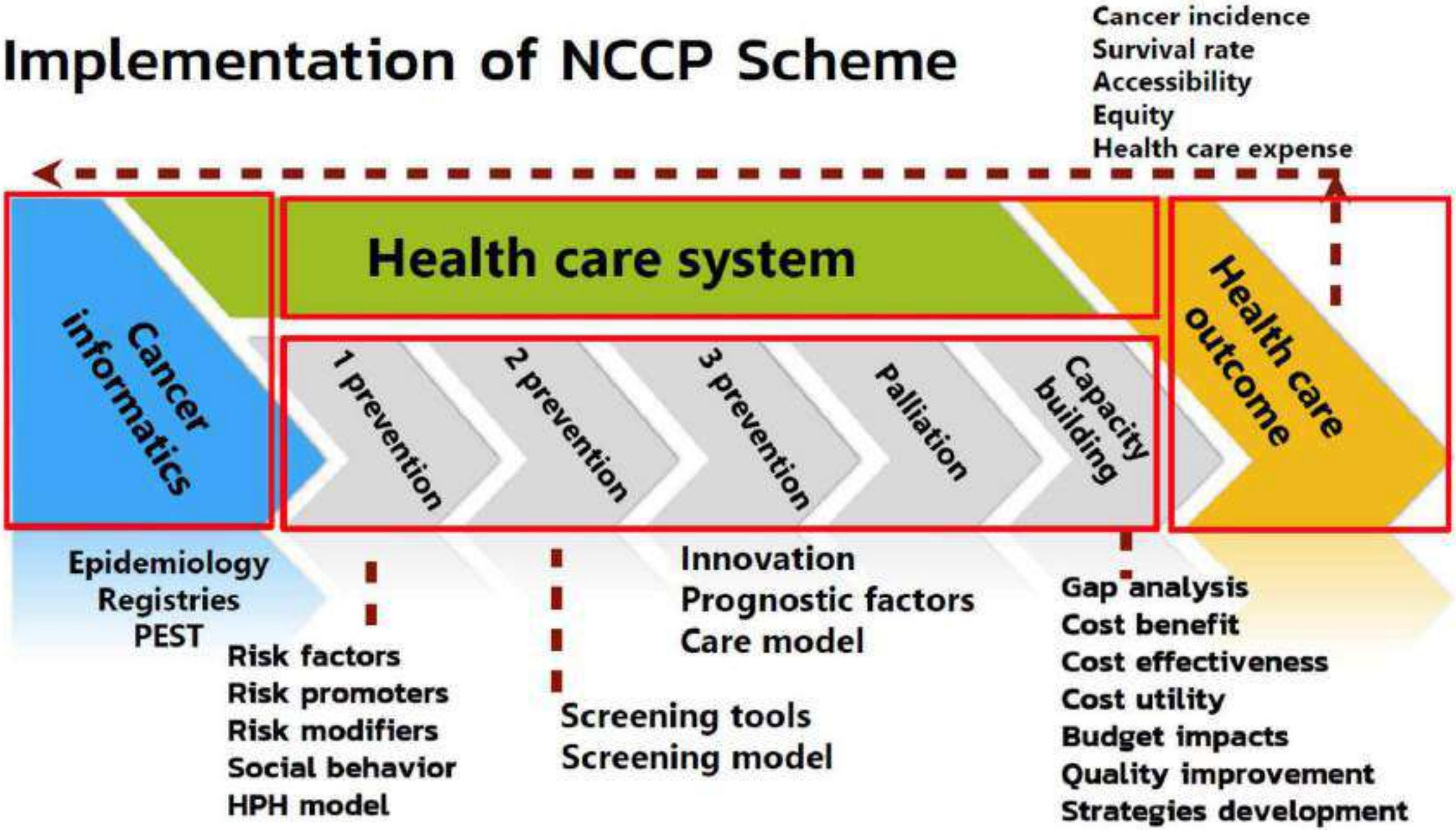
Hepatocellular Carcinoma surveillance and management across APAC

Somchai Thanasitthichai, MD, FRCST

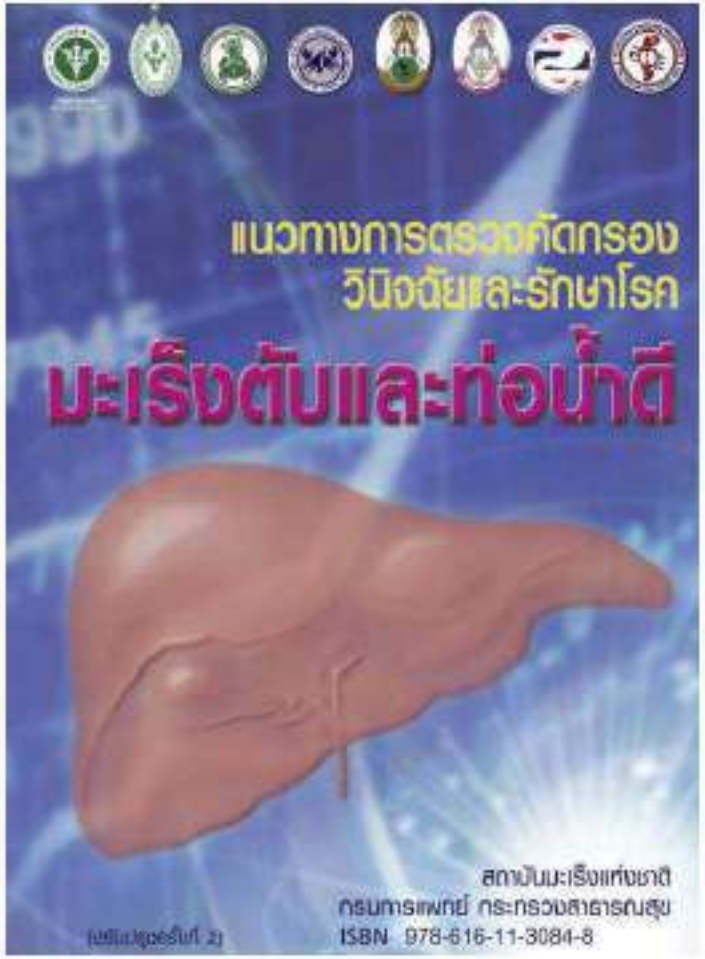
Director of National Cancer Institute

Department of Medical Sciences
Ministry of Public Health
Thailand

Implementation of NCCP Scheme



Surveillance and Management



Identification of At-Risk Populations (1)

- Persons with cirrhosis, regardless of age or other risk factors
- Persons with chronic hepatitis B, especially males over 40, females over 50, and those with a family history of HCC
- Persons with chronic hepatitis C infection at fibrosis stages 3 and 4

Regular Surveillance and Screening

- Ultrasound and AFP testing every 6-12 months

Research study on cost-effectiveness analysis of AFP and liver ultrasound for HCC surveillance in Thailand

"Cost-effectiveness of Alpha-fetoprotein and Liver Ultrasound for semi-annual Hepatocellular Carcinoma Screening in Human with Hepatitis B Surface Antigen Positive or Patients with Chronic Hepatitis B"

Not cost-effective for semi-annual screening HCC in patients with hepatitis B surface antigen positive or patients with chronic hepatitis B

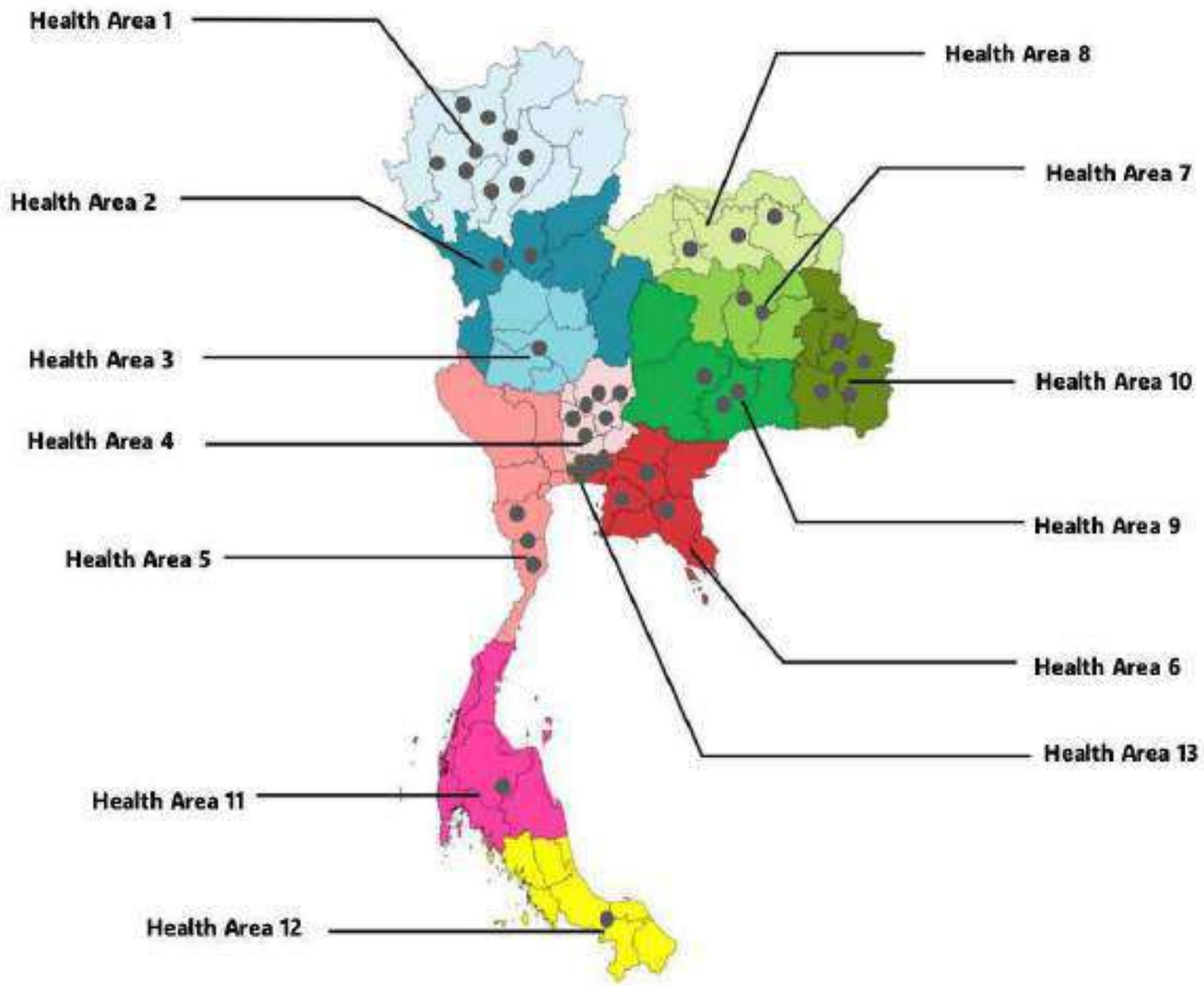
- *Semi-annual HCC screening had an incremental cost-effectiveness ratio (ICER) of 471,320 baht per QALY for males and 560,336 baht per QALY for females compared to no screening*
- *Thai threshold that ICER of cost-effective intervention should not be exceed 300,000 baht per QALY.*

Sources:

(1) Clinical Practice Guidelines for screening, diagnosis, and treatment of liver and bile duct cancer, National Cancer Institute, Thailand

(2) Attasit (2008), Cost-effectiveness of Alpha-fetoprotein and Liver Ultrasound for semi-annual Hepatocellular Carcinoma Screening in Human with Hepatitis B Surface Antigen Positive or Patients with Chronic Hepatitis B, Institute of Medical Research and Technology Assessment, Department of Medical Services

Liver Center (52)



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Lunch

APAC Hepatocellular Carcinoma Policy Forum 2024

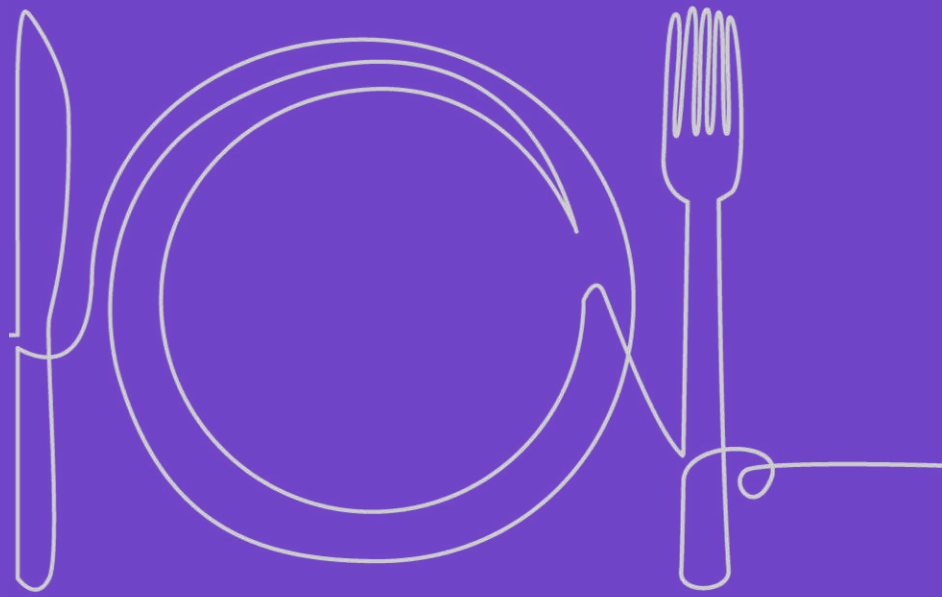

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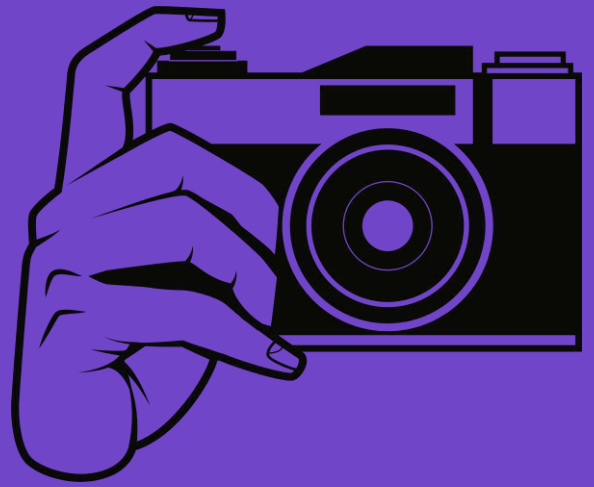
Photo Session

APAC Hepatocellular Carcinoma Policy Forum 2024



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Panel 2

Success Stories: Effective Practices in HCC Surveillance and Management

Ms. Roberta Sarno (Moderator)
Director
APAC Liver Disease Alliance

Prof. Chien-Jen Chen
Academician & Distinguished Professor,
Genomics Research Center, Academia Sinica
Taiwan

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Dr. Norlen Bin Mohamed
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Non-Communicable Disease Sector, Disease Control Division
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Malaysia

Dr. Poowanai Sarkhampee
Hepato-Pancreato-Biliary Surgeon, Senior Professional Level
Division of Hepato-Pancreato-Biliary Surgery and Transplantation, Sunpasitthiprasong Hospital
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APAC Hepatocellular Carcinoma Policy Forum 2024

Bangkok October 2, 2024

Success story:

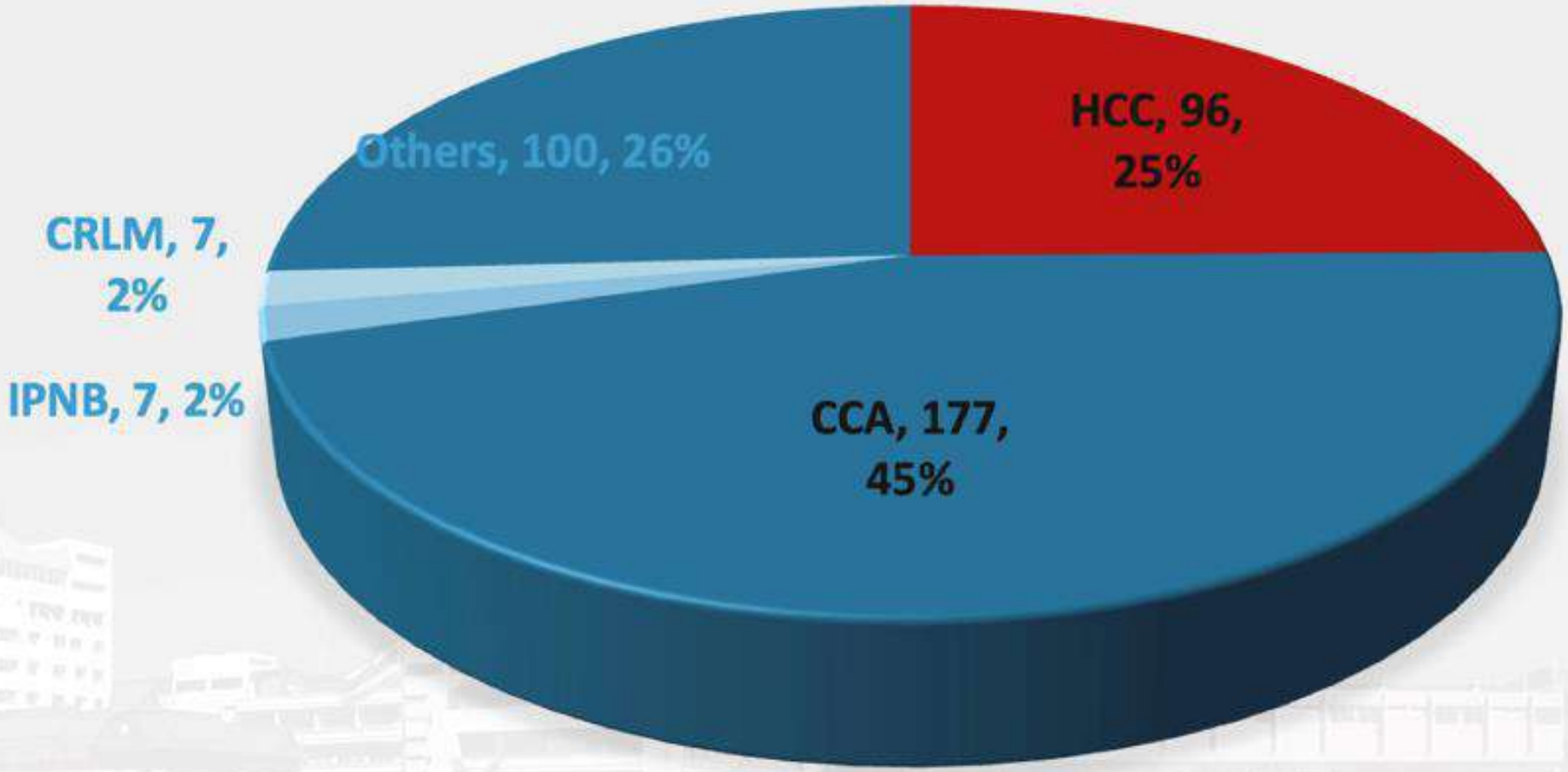
Effective practices in HCC surveillance and management

Surgeon's perspective.

Dr. Poowanai Sarkhampee, MD, FRCST

Division of Hepato-Pancreato-Biliary and Transplantation
Department of Surgery, Sunpastthiprasong Hospital
Ubon Ratchathani, Thailand

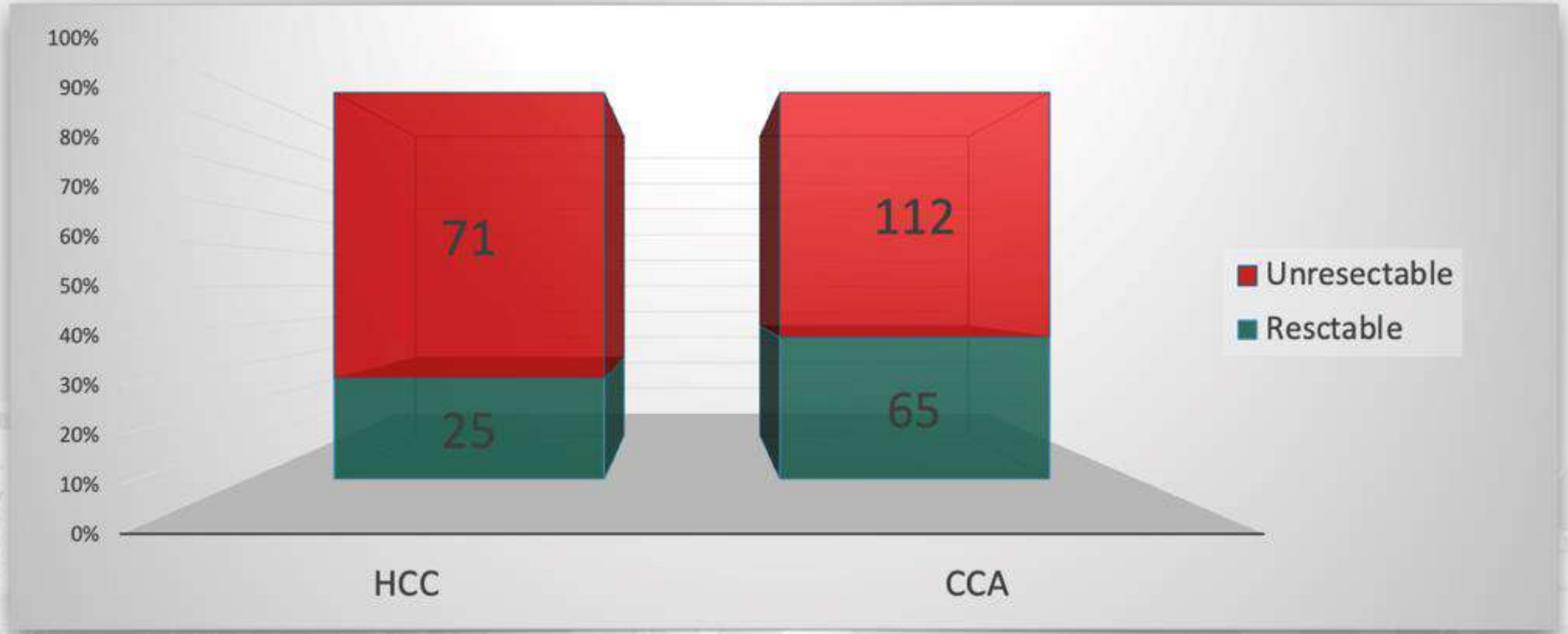
HPB malignancy cases at Surgical OPD Sunpasitthiprasong Hospital (6 months)



Unpublished data from Sunpasitthiprasong Hospital, January 2024 - June 2024

Poowanai Sarkhampee, MD, FRCST

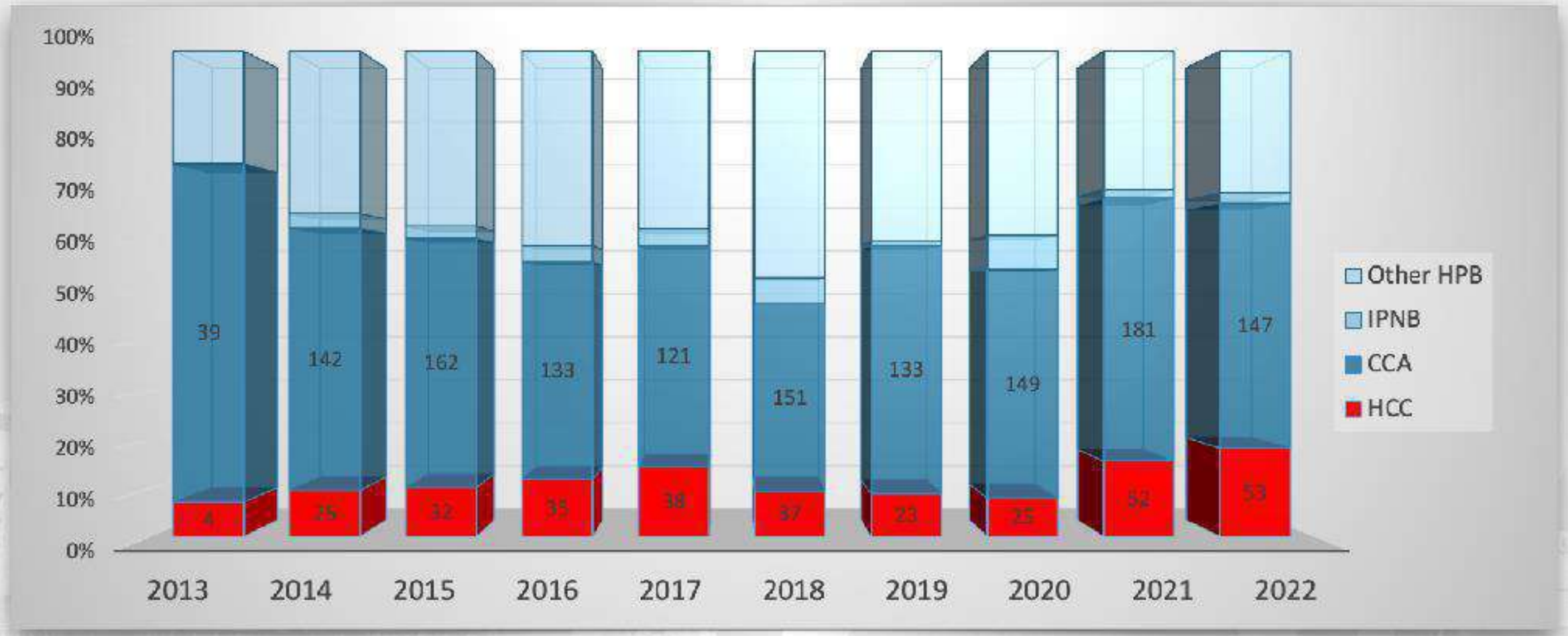
HPB malignancy cases at Surgical OPD Sunpasitthiprasong Hospital (6 months)



Unpublished data from Sunpasitthiprasong Hospital, January 2024 - June 2024

Poowanai Sarkhampee, MD, FRCST

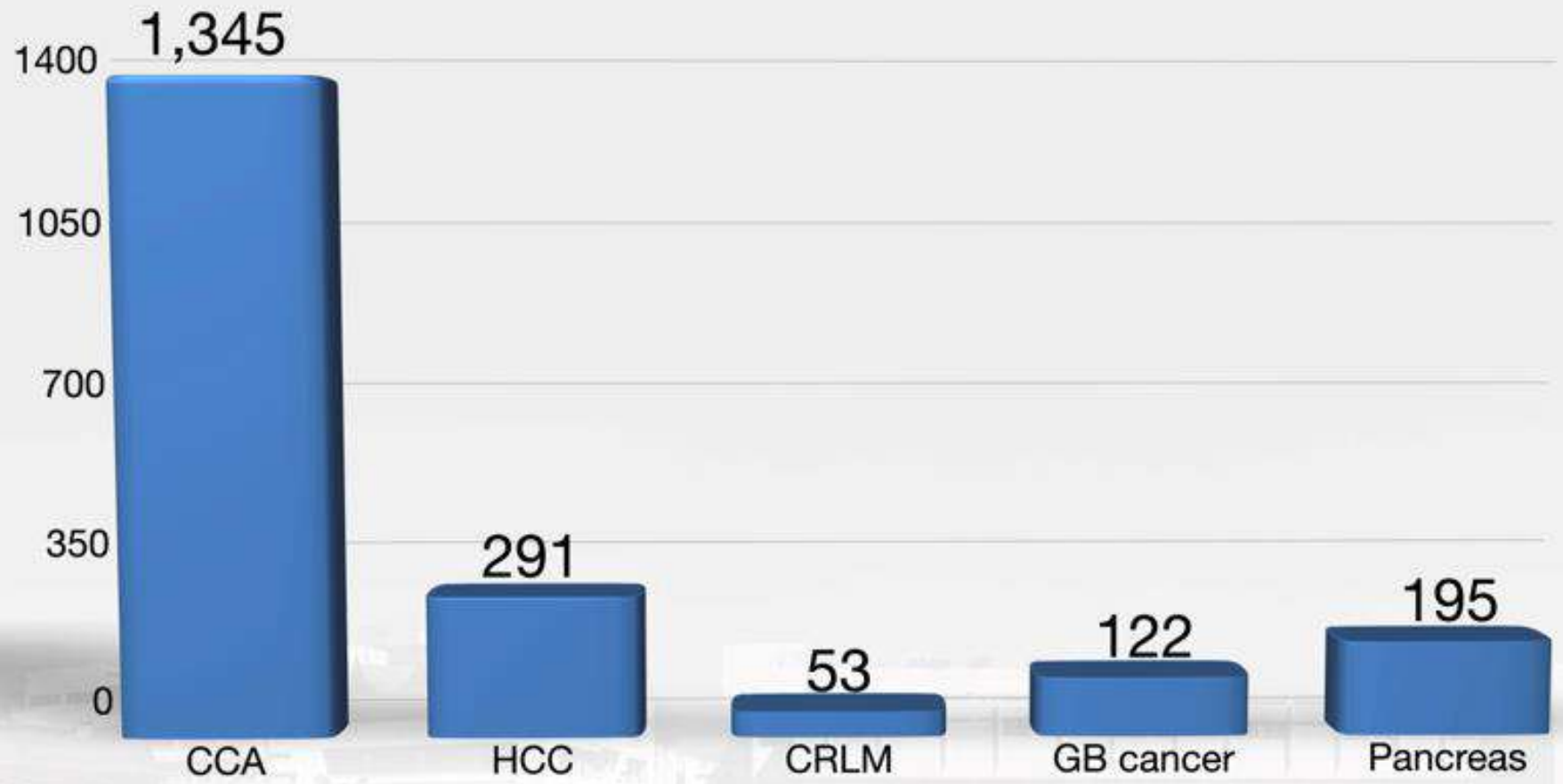
HPB patients underwent Surgical treatment at SPSH



Unpublished data from Sunpasitthiprasong Hospital, October 2013 - December 2022

Poowanai Sarkhampee, MD, FRCST

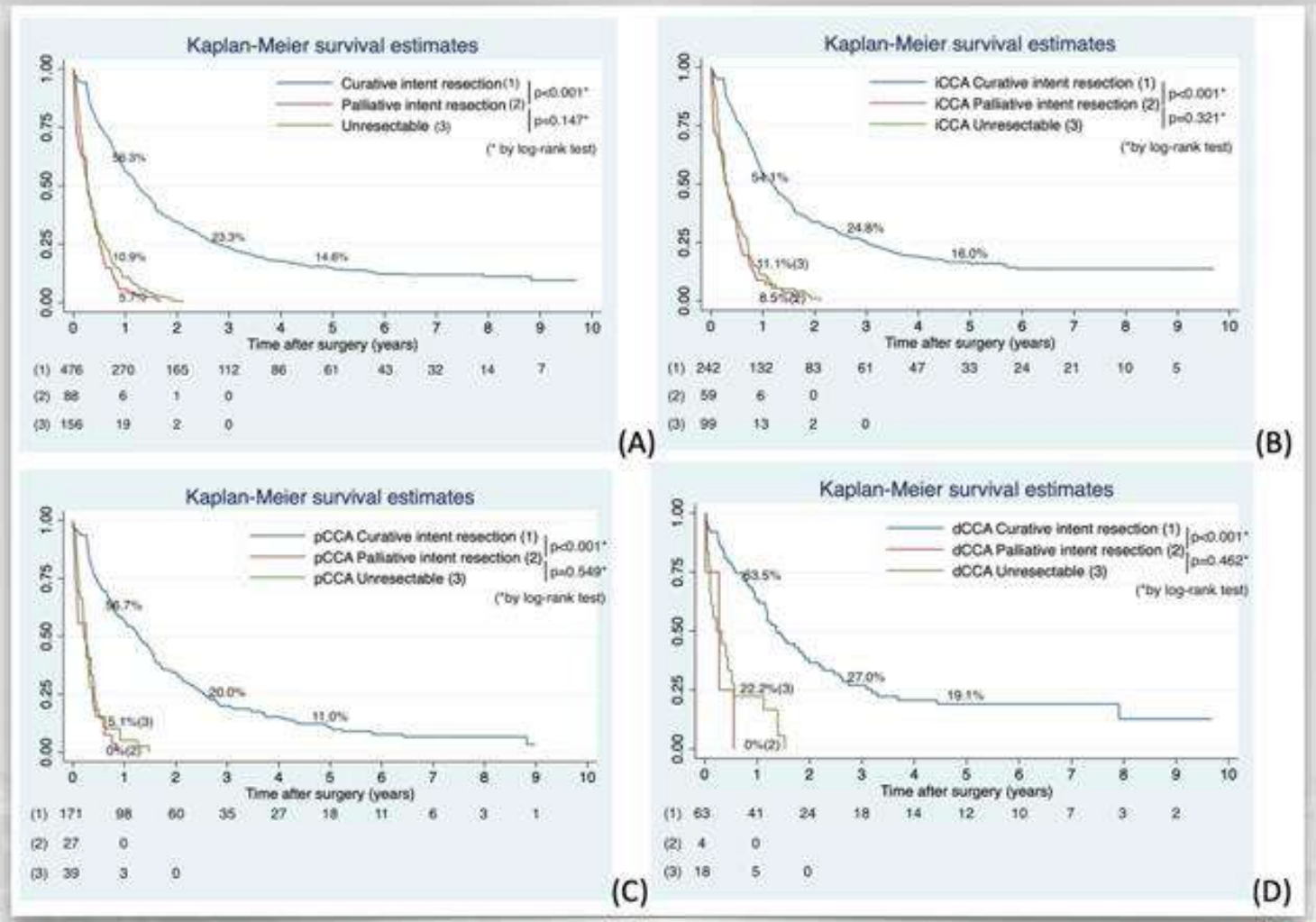
HPB patients underwent
Surgical treatment (2013-2022)



Unpublished data from Sunpasitthiprasong Hospital, October 2013 - December 2022

Poowanai Sarkhampee, MD, FRCST

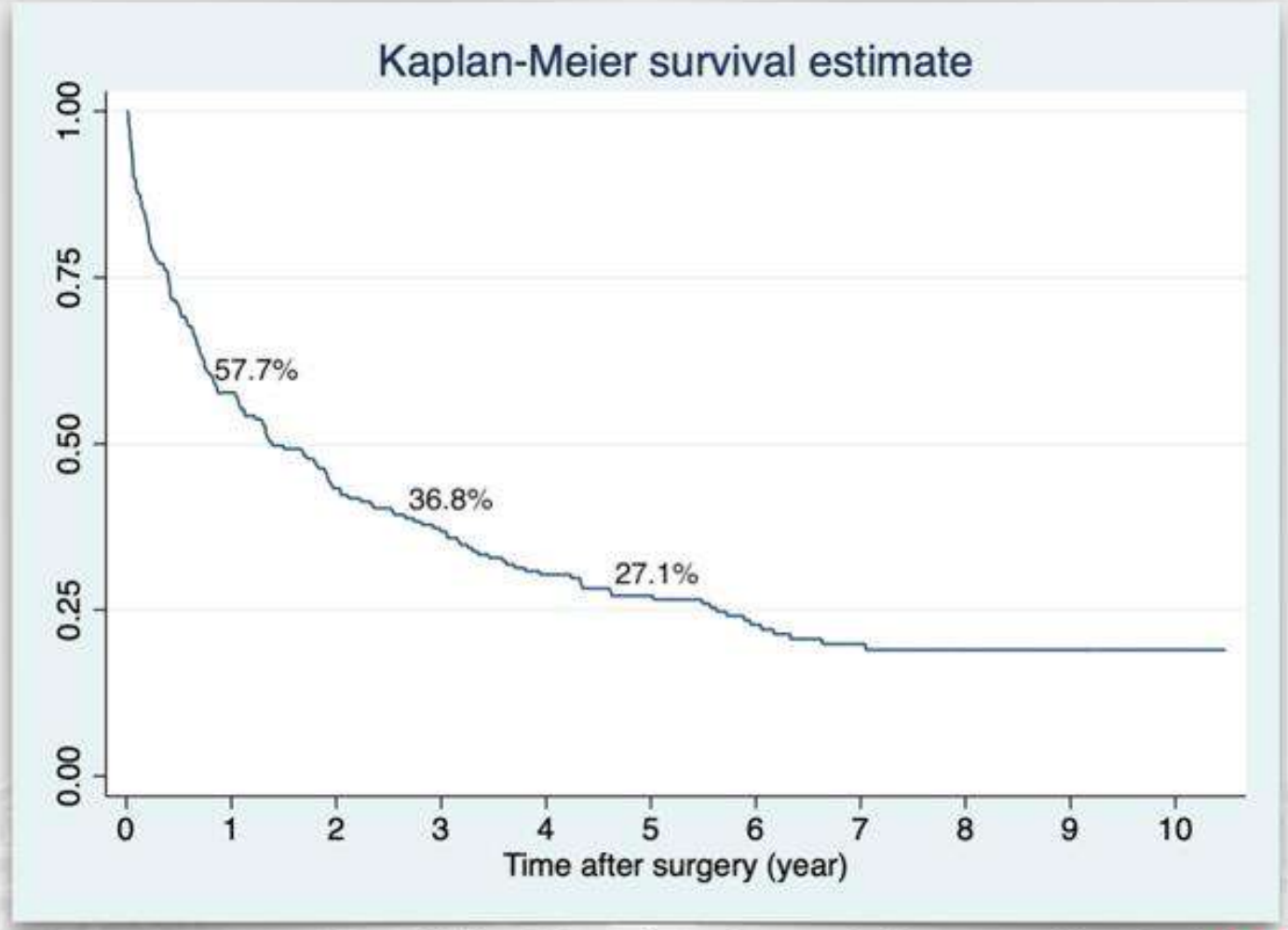
Overall Survival of CCA underwent surgery (Data from 2013-2018)



Unpublished data from Sunpasitthiprasong Hospital, October 2013 - December 2018

Poowanai Sarkhampee, MD, FRCST

Overall Survival of HCC underwent resection (Data from 2013-2018)



Unpublished data from Sunpasitthiprasong Hospital, October 2013 - December 2018

Poowanai Sarkhampee, MD, FRCST

Prevention and early detection of patients are key success factors of cancer treatment.

Poowanai Sarkhampee, MD, FRCST

Cancer Warriors

Poowanai Sarkhampee, MD, FRCST

Cancer Warriors

Cancer Warrior
สำนักงานปลัดกระทรวงสาธารณสุข

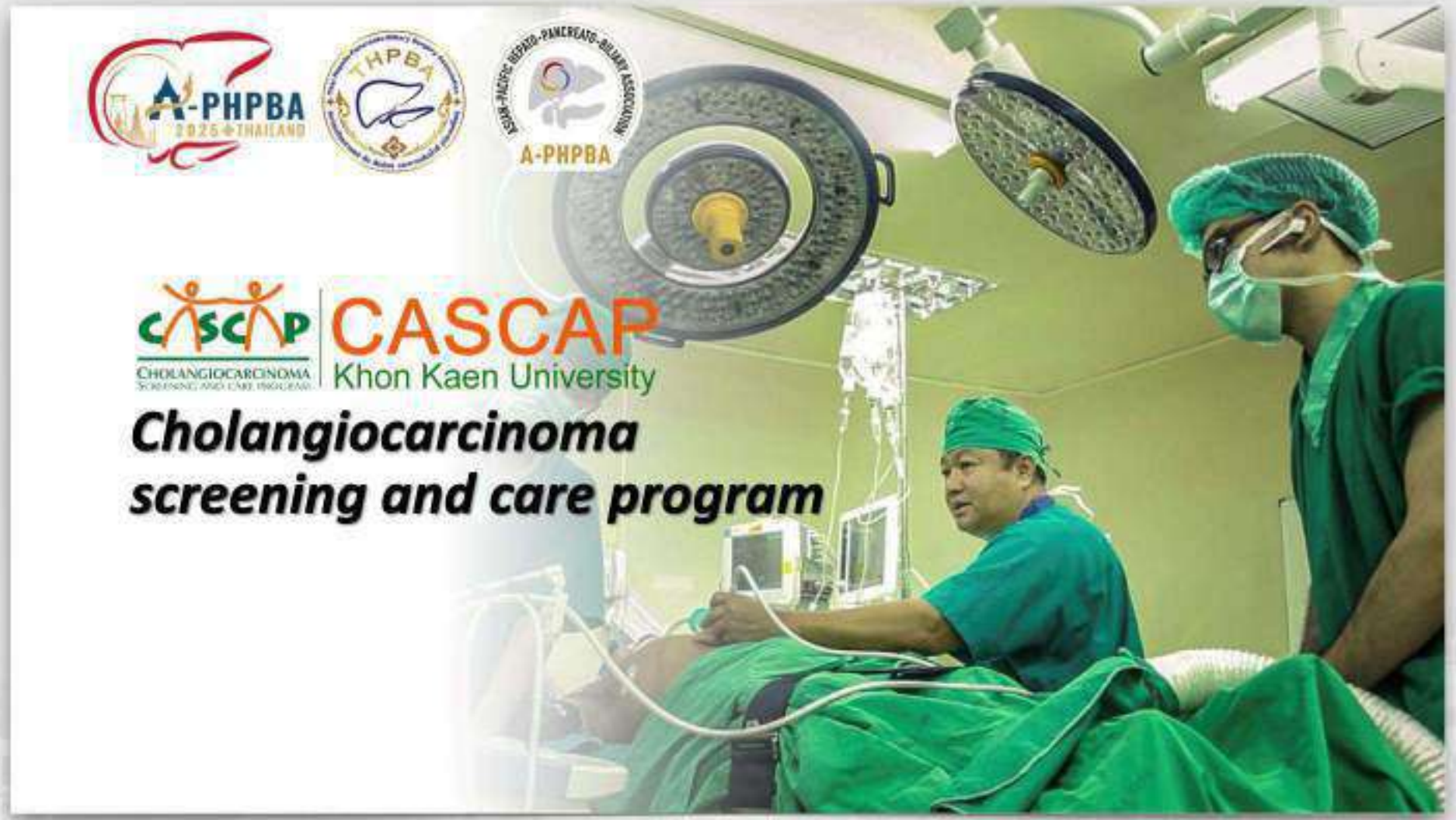
ประเด็น	ชื่อ	ตำแหน่ง	หน่วยงาน
Colon	นายแพทย์วิบูลย์ ภัณฑบดีกรณ์	รองผู้อำนวยการ	รพ.พหลพลพยุหเสนา
Cervix	ว่าที่ร้อยตรี ดร.นายแพทย์วัชรินทร์ เฉิดฉิ้ม	ผู้ช่วยผู้อำนวยการด้านวิจัยและพัฒนา	รพ.พระปกเกล้า
Breast	นายแพทย์นพวัชร์ สมานคติวัฒน์	หัวหน้ากลุ่มงานศัลยกรรม	รพ.ราชบุรี
Cholangiocarcinoma	นายแพทย์ภูวนัย สาคำภีร์	นายแพทย์ชำนาญการพิเศษ	รพ.สรรพสิทธิประสงค์
HCC	รศ.(พิเศษ)นพ.อรุณชัย แซ่ฉั่ง	นายแพทย์ชำนาญการพิเศษ	รพ.หาดใหญ่

Cancer Warriors

Hepatoma

ประเด็น	กิจกรรม	กลุ่มเป้าหมาย	เป้าหมาย
Situation and Natural History of Disease	- มะเร็งอันดับหนึ่งของประเทศไทย(รวมมะเร็งท่อน้ำดี) มีผู้ป่วยรายใหม่ 27,394 ราย/ปี และเสียชีวิต 26,704 ราย/ปี(2563) - สาเหตุหลักเกิดจากตับอักเสบจากสาเหตุต่าง ๆ เช่น ไวรัสตับอักเสบ บี และ ซี		
Primordial Prevention	- Life style medicine - ส่งเสริม Safety Sexual Intercourse - ส่งเสริมพฤติกรรมการกิน - ฉีดวัคซีน HBV ในเด็กแรกคลอด	HBV vaccination ในเด็กแรกเกิดทุกคน	
Primary Prevention	- ตรวจคัดกรองไวรัสตับอักเสบบีและซี ด้วย rapid test - ผู้ป่วย HCV ให้การรักษาด้วยยา SOF/VEL 12 week	ประชากรอายุ 35-55 ปี	จำนวน 1,000,000 ราย ต่อปี
Secondary Prevention	- ultrasound screening	ผู้ป่วยที่มีผลการคัดกรองผิดปกติ	Ultrasound - HCV 4,500 ราย - HBC 10,000 ราย
Tertiary Prevention	- Early stage : Ablation/Resection/Transplant/Ablation - Late stage : TACE/Targeted Tx	ผู้ป่วยที่ตรวจพบมะเร็ง	จำนวน 400-600 คน/ปี
Palliative Care	ร่วมกับ SP ชีวาภิบาล	ผู้ป่วยที่ไม่ตอบสนองต่อการรักษา/ระยะสุดท้าย	

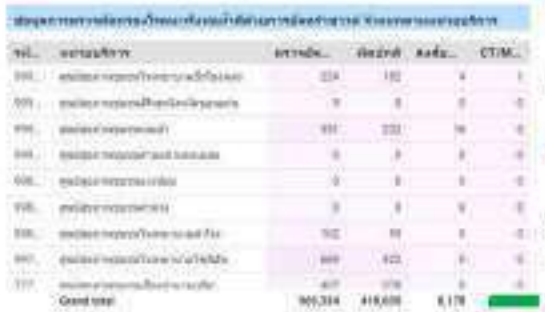
CASCAP



Poowanai Sarkhampee, MD, FRCST

CASCAP

Screening ultrasound 2013-2023



Result

CCA 01

1,786,843

Total U/S

969,334 times

852,415 persons

Abnormal

418,630(49.1%)

Suspected CCA

8,178(0.96%)

Poowanai Sarkhampee, MD, FRCST

Hepatocellular Carcinoma Free

Thailand

Integration

The action or process of successfully joining or mixing with a different group of people.

Collaboration

The situation of two or more people working together to create or achieve the same thing.

Sustainability

The quality of being able to continue over a period of time.

Knowledge

Facts, information, and skills acquired by a person through experience or education; the theoretical or practical understanding of a subject.

Poowanai Sarkhampee, MD, FRCST

Panel 2

Success Stories: Effective Practices in HCC Surveillance and Management

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Director
APAC Liver Disease Alliance

Prof. Chien-Jen Chen
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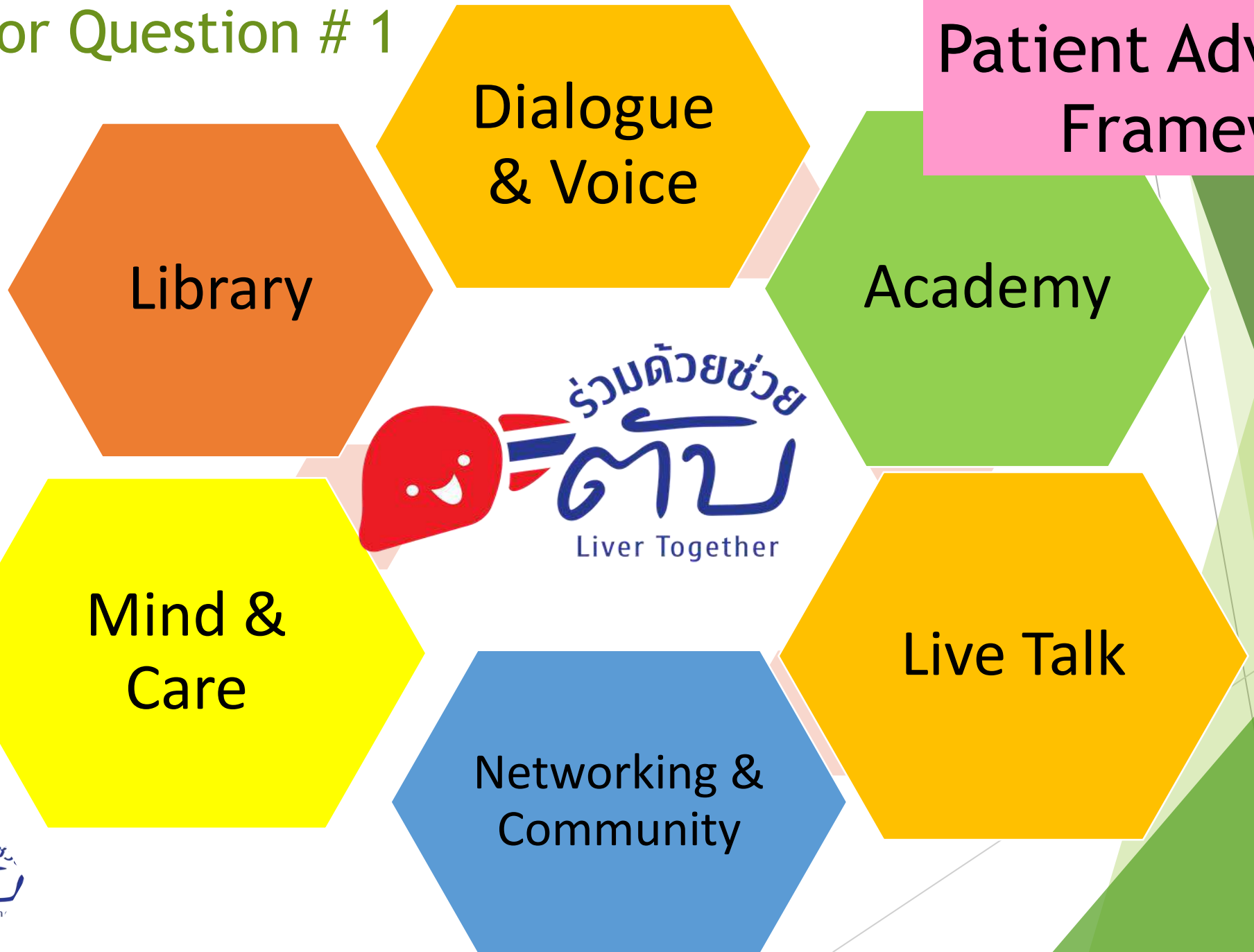
ร่วมด้วยช่วย ตับ

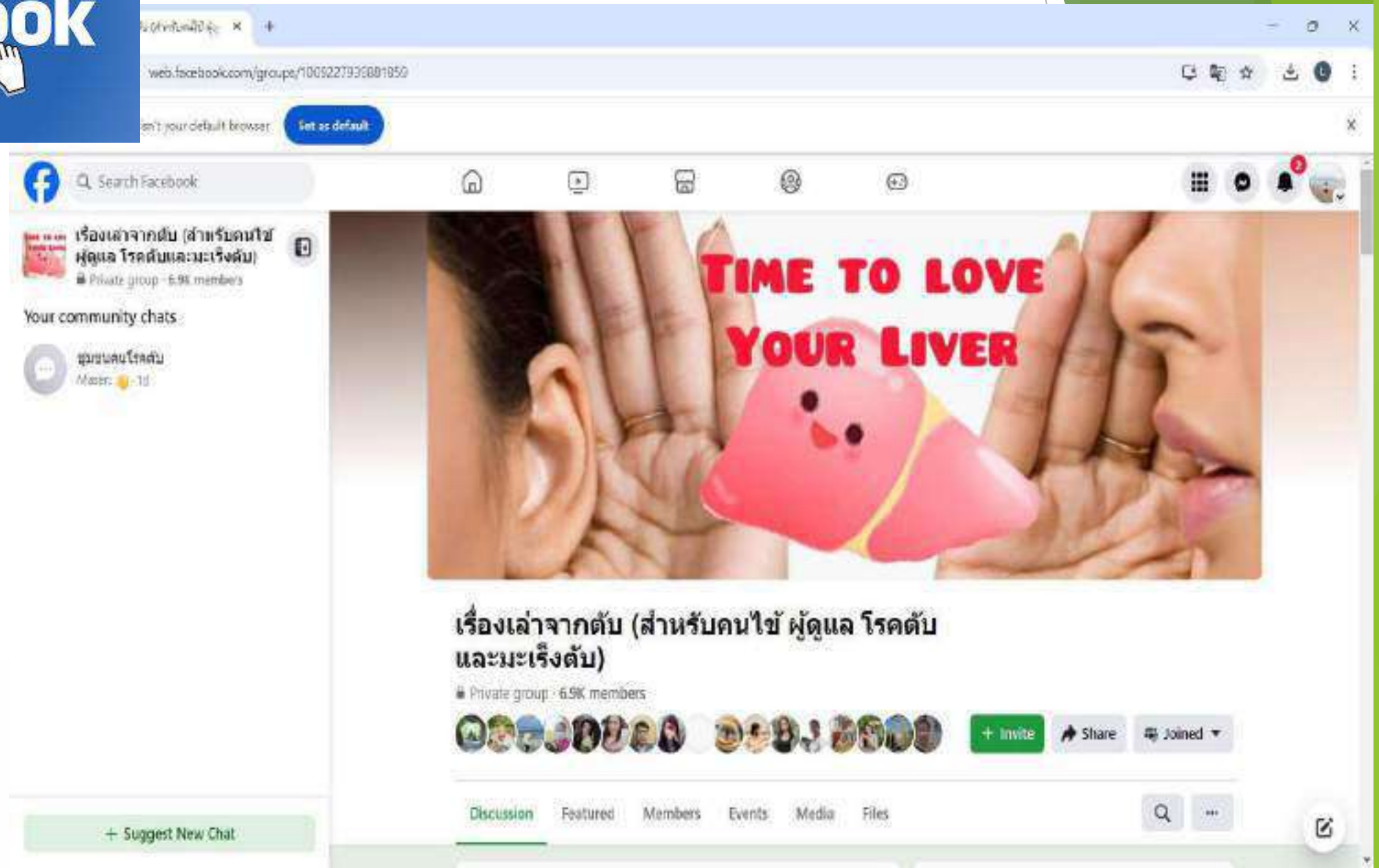
Liver Together

Answer for Question # 1

Patient Advocate's Framework

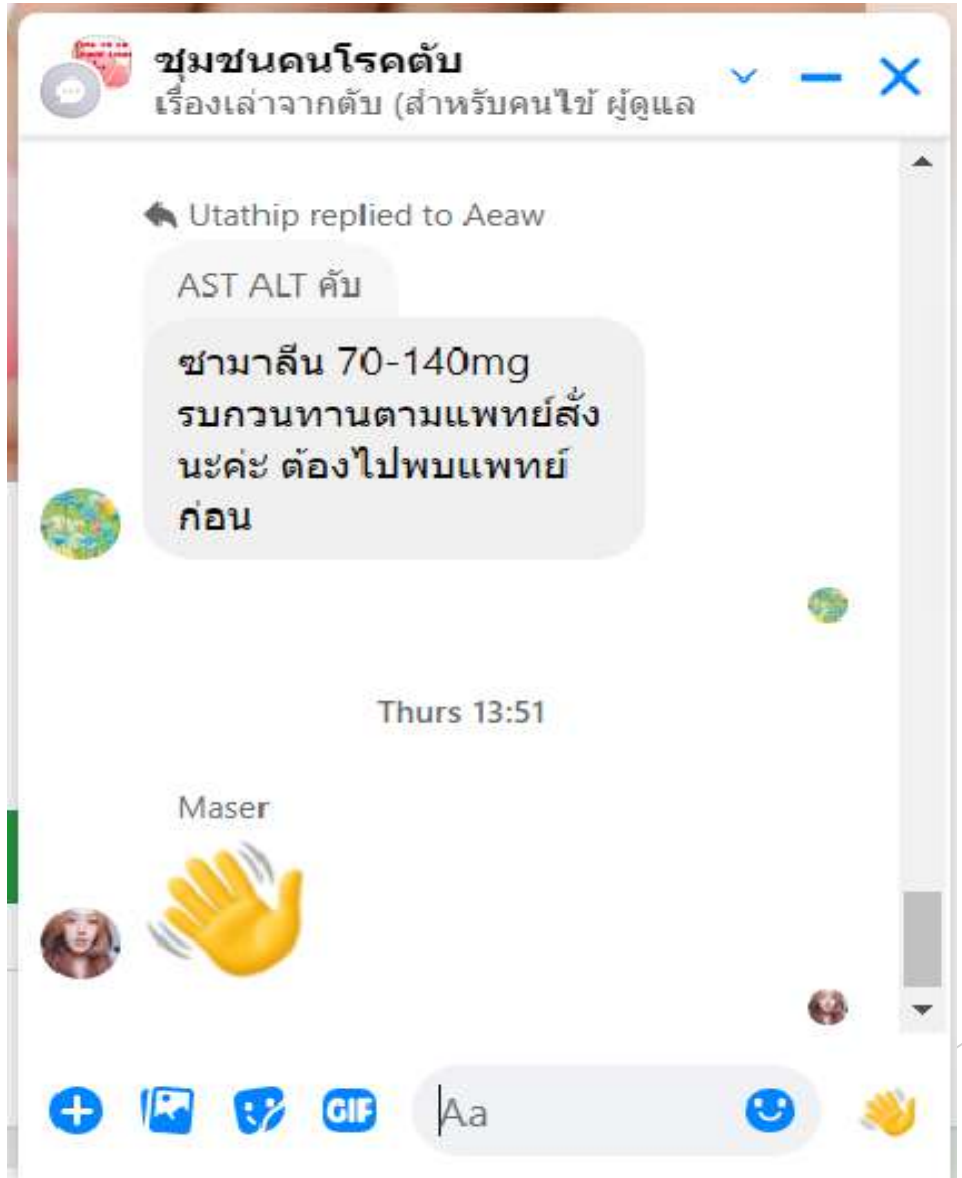


facebook



ร่วมด้วยช่วยตับ
Liver Together

Chat Community



ร่วมด้วยช่วยตับ
Liver Together

ร่วมด้วยช่วย ตับ
Liver Together

LIVE

Answer for Question # 2
What do patients need most from their healthcare system to improve their outcomes?

- To facilitate them to get reach and readiness helping them from “early step” to “last step” of their patient journey to meet their expectations.
- To continue promoting HCC Screening campaigns + Early HCC diagnosis for all risk groups (test and treat strategies)

In the Thailand context, the Thai health care system should do..

- Proactive communication to employers for them to well understand how to help their test-positive employees with job applications and how to carry on.

- Expansion of the clinical channels all over the country to enable better access to certain medicines, including those who are the most effective, and with affordable prices for full medical treatments.

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HCC APAC
Policy Forum Workshop

APAC Liver Disease Alliance

Disclaimer: The slides shared in this section are work-in-progress investigations into current state and next steps for 7 health systems and **DO NOT** represent any government or health system policy or committed plans. These are also **PRIVATE & CONFIDENTIAL** – do not share with anyone outside of the direct attendee list, unless within your own health system with permission of all of your group.

The HCC APAC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

Workshop Agenda

Session type	Session	Led by
Short speech – 5 min	**Opening remarks**	Roberta Sarno (APAC Liver Disease Alliance)
Plenary - 10 min	**Presentation on challenges and recommendations along the patient journey** (from White Paper)	Will Brown (Vista Health)
	Presentation on Japan best practices (from Prof Kudo's paper)	
Workshop breakout – 75 min	**Brainstorming solutions to existing regional issues** (incl. prioritization based on feasibility, inclusivity and impact) • Session 1: Awareness and Prevention (25 min) • Session 2: Early detection and Diagnosis (25 min) • Session 3: Access to treatment (25 min)	Roberta Sarno (APAC Liver Disease Alliance) Will Brown (Vista Health) Colin Tan (Vista Health) Yongho Yi (Deloitte) Tran Nguyen (Sophie, Deloitte) Phat Parkpien (APCO)
Feedback presentation and Q&A – 25 min	**Playback of solutions from each group with short Q&A**	Participants
Short speech – 5 min	**Conclusion and closing remarks**	Roberta Sarno (APAC Liver Disease Alliance) and Will Brown (Vista Health)

Australia

See also:

- Roadmap to Liver Cancer Control 2023 – 2,5 and 10 year roadmap
- Clinical practice guidelines for HCC surveillance 2023
- Optimal care pathways for HCC
- Australian Cancer Plan
- National HCV/HBV/Obesity/Diabetes Strategies

PATIENT JOURNEY STAGE	CHALLENGE	HOW CRITICAL IS IT TO ADDRESS THIS CHALLENGE?	POTENTIAL SOLUTION(S)	RESPONSIBLE AGENCY / DEPARTMENT
AWARENESS	• Indigenous • CALD • Diabetes/obesity	10	• Co-design with affected communities • Double diamond	• Government (national, jurisdictional, cancer council) • Stakeholders – patients • Researchers
PREVENTION	• Alcohol use • Obesity/diabetes – • Viral hepatitis diagnosis -> treatment	10	• Alcohol policy – advertising, minimum pricing • Sugra policy/taxes • Diagnosis of HCV/HBV in all at-risk • Education primary care	
EARLY DETECTION	• Access to US, expand US-based screening - dedicated ultrasonographers, multi-screening trucks to regional areas • Diagnosis in primary care • Poor performance of US in obesity etc	10	• Expand US screening • Blood-based biomarkers – GAAD • Risk stratification tools • Identification of liver disease in primary care + referral pathways • National screening programme – all cirrhosis, HBV –age	
DIAGNOSIS	• Access to MRI • Patient support	10	• Cost effectiveness • Funding/MSAC • Screening strategy • Liver nurses • Patient support line and navigation	
ACCESS TO TREATMENT	• Equity/geography • Access to funded 2nd line systemic therapies • HCC managed by non-oncologists	10	• Australian cancer plan • Access to MDTs • Cancer care networks	

India

PATIENT JOURNEY STAGE	CHALLENGE	HOW CRITICAL IS IT TO ADDRESS THIS CHALLENGE? [*on a scale of 10*]	POTENTIAL SOLUTION(S)	RESPONSIBLE AGENCY / DEPTARTMENT
AWARENESS	• Interpersonal communication. Awareness is existing but the one-on-one communication needs to be scaled up. Some patients do not change their behaviors despite the awareness efforts (for example alchol consumption, obesity)	*TBD*	• *Scale up the existing counselling services (integrated for efficiency). There are already counsellors under the current programs, but it would be good to have counsellors trained to address integrated health priorities/programs (to increase efficiency/reduce costs)*	• *Community health center led by a CMO (Chief Medical Officer) at block level which is under the district level*
PREVENTION	• Challenges due to geographic diversity, with difficulties in reaching geographically isolated and disadvantaged patients (who then have issues to access)		• Instead of giving a month therapy, we allow a longer supply (lesson learned from COVID-19)	
EARLY DETECTION				
DIAGNOSIS				
ACCESS TO TREATMENT	• Pediatric formulation does not exist because of the age threshold • Affordable RUP (Re-Use Prevention syringes)		• Request to the manufacturer to develop (investment in R&D) • Negotiate price reduction with manufacturers	

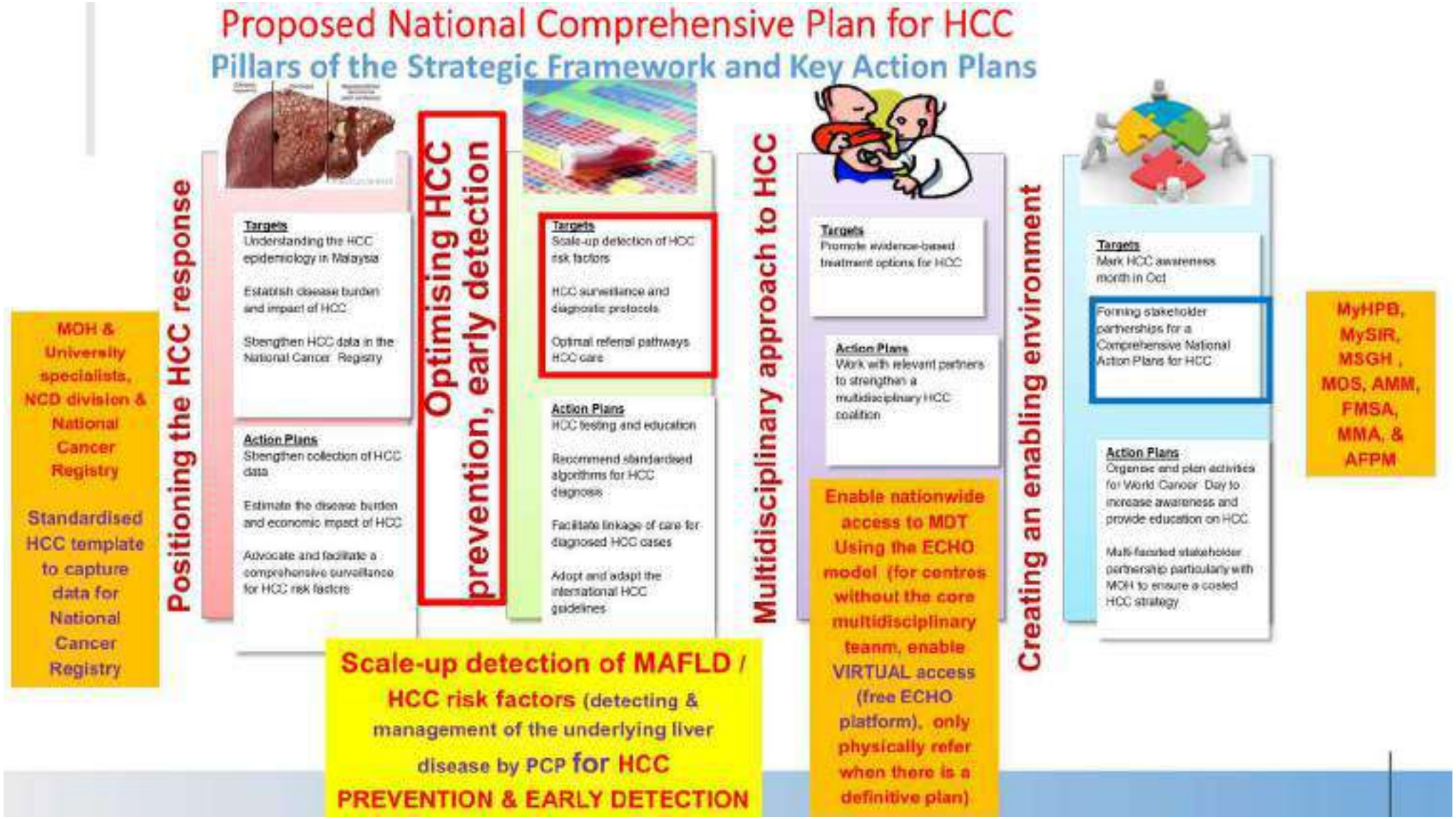
South Korea

PATIENT JOURNEY STAGE	CHALLENGE	HOW CRITICAL IS IT TO ADDRESS THIS CHALLENGE? [*on a scale of 10*]	POTENTIAL SOLUTION(S)	RESPONSIBLE AGENCY / DEPTARTMENT
AWARENESS	• *Lack of awareness activities of general public*	*9*	*1. KLCA already runs awareness programs* *2. Government initiative is needed*	• *MOH*
PREVENTION	• Previously challenge: lack of Hep C national screening program	9	• New policy/screening program introduced in 2024	• *MOHW* • *KDCA*
EARLY DETECTION	• *HCC guideline: Single biomarker (AFP) is recommended*	*10*	• *Update the HCC guideline*	• *KLCA* • *MOHW*
DIAGNOSIS	N/A	10	N/A	
ACCESS TO TREATMENT	• Reimbursement is limited	8	• Expansion of reimbursement	• NHIS • MOHW • Pharma companies

Malaysia (1/2)

PATIENT JOURNEY STAGE	CHALLENGE	HOW CRITICAL IS IT TO ADDRESS THIS CHALLENGE? [*on a scale of 10*]	POTENTIAL SOLUTION(S)	RESPONSIBLE AGENCY / DEPARTMENT
AWARENESS	• Awareness to HCPs (outside of hepatologists) • Awareness to possible at-risk of patients (also need to better understand who is at risk) • Awareness to lab personnel (make the tests available)	9	• Advocacy programme to policymakers on HCC • Strengthen national cancer registry	• AMM (Academy of Medicine Malaysia)/ specialists/MoH • All other clinical stakeholders
PREVENTION	• Treating identified Hep B&C/ MALFD/Alchohol	10	• Integrating HCC risk factors with NCD screening programmes	• Primary care stakeholders • MoH • AFPM • AMM • CSO • MMA
EARLY DETECTION	• Early detection of high-risk groups • Scaling up detection of HCC risk factors	10	• Surveillance for early detection of HCC in identified high risk groups > prompt for referral – EMR?	• All tertiary centres • MoH
DIAGNOSIS	• Made in an MDT setting – ensures access to care and treatment • MDT approach	9	• Minimum requirement (ECHO model) – virtual MDTs (IR, gastro/hepato, HPB, oncologist) • Value-based approach to policymakers (template model) to access evidence-based treatment	• Key tertiary centres with multidiscipline
ACCESS TO TREATMENT	• Evidence-based treatment options	9		

Malaysia (2/2)


Proposed National Comprehensive Plan for HCC
Pillars of the Strategic Framework and Key Action Plans
Positioning the HCC response
Optimising HCC prevention, early detection
Multidisciplinary approach to HCC
Creating an enabling environment
Targets
Understanding the HCC epidemiology in Malaysia
Establish disease burden and impact of HCC
Strengthen HCC data in the National Cancer Registry
Action Plans
Strengthen collection of HCC data
Estimate the disease burden and economic impact of HCC
Advocate and facilitate a comprehensive surveillance for HCC risk factors
Targets
Scale-up detection of HCC risk factors
HCC surveillance and diagnostic protocols
Optimal referral pathways HCC care
Action Plans
HCC testing and education
Recommend standardised algorithms for HCC diagnosis
Facilitate linkage of care for diagnosed HCC cases
Adopt and adapt the international HCC guidelines
Targets
Promote evidence-based treatment options for HCC
Action Plans
Work with relevant partners to strengthen a multidisciplinary HCC coalition
Targets
Mark HCC awareness month in Oct
Forming stakeholder partnerships for a Comprehensive National Action Plans for HCC
Action Plans
Organise and plan activities for World Cancer Day to increase awareness and provide education on HCC
Multi-faceted stakeholder partnership particularly with MOH to ensure a costed HCC strategy
MOH & University specialists, NCD division & National Cancer Registry
Standardised HCC template to capture data for National Cancer Registry
Scale-up detection of MAFLD / HCC risk factors (detecting & management of the underlying liver disease by PCP for HCC PREVENTION & EARLY DETECTION
Enable nationwide access to MDT Using the ECHO model (for centres without the core multidisciplinary teamm, enable VIRTUAL access (free ECHO platform), only physically refer when there is a definitive plan)
MyHPB, MySIR, MSGH , MOS, AMM, FMSA, MMA, & AFPM

Taiwan

PATIENT JOURNEY STAGE	CHALLENGE	POTENTIAL SOLUTION(S)	RESPONSIBLE AGENCY / DEPTARTMENT
AWARENESS	• **General population** and high risk groups are unfamiliar with common hepatitis and HCC risk factors (e.g. Cardiometabolic risk factors) • NBNC patients (resolved HBV, MASLD, ALD) => fibrosis is an issue, should promote fibrosis evaluation	• Personalized health education messaging through APPs (what patients should do instead of what patients should not do) • Cardiometabolic risk factors high risk screening, not general population screening • Generate model for risk prediction for at risk MASLD patients • Provide information and health checkup from the company/work • Health promotion agency provide health checkup results for Bureau of National Health Insurance agency • Cross department data sharing (HPA vs BNHI) by standardized FHIR system, but protected by personalized privacy protection low	• *HPA, Ministry of Labor with special budget*
PREVENTION	• MASLD patients management plan could be better → unaware that this could lead to HCC	• Metabolic syndrome control/management plan or campaign. (if reduce risk factor, iphone lot drawing) • Health promotion exercise/Gyms • exercise for social/ => health • Social media choosing • Gamification!! Checking to health education video, then get points • spill-over insurance (reduction of insurance fee)	• *NHI*
EARLY DETECTION **DIAGNOSIS**	• Reimbursed US + AFP + PIVKAII surveillance is only available to a limited patient population	• *High risk patient calculator to clarify and define high risk patient groups who can benefit from US + AFP + PIVKAII (from a cost effectiveness perspective)*	
ACCESS TO TREATMENT	• Reimbursement for new ICI therapy is limited to intermediate/advanced HCC, and patients can only obtain reimbursement once • Limited input from patient groups in reimbursement decisions (i.e. merely observers, and limited to treatment assessment)	• Establish framework to increase patient group involvement, especially in identifying treatments that should be considered for reimbursement • Increase publicity for patient groups and their in-depth knowledge of economic and social cost of HCC to raise policymakers and payers' awareness of the importance of patient group input	• NHI

Thailand

PATIENT JOURNEY STAGE	CHALLENGE	HOW CRITICAL IS IT TO ADDRESS THIS CHALLENGE? [*on a scale of 10*]	POTENTIAL SOLUTION(S)	RESPONSIBLE AGENCY / DEPTARTMENT
AWARENESS	• Lack of updated knowledge among GPs • Lack of awareness in young population • Lack of continuity in government policy	8	• Training in medical schools / young HCPs • Segmented social media campaign + health education curriculum reform • Drive HCC as national agenda	• MOPH • Royal college • ThaiHealth • Government
PREVENTION	• Fragmented public health system • HBV VL cannot be reimbursed in adults • Early detection in high-risk adults	7	• HBV VL should be reimbursed • Encourage screening in adults • Increase hepatitis-related clinics nationwide at local/community level • Increase training among GPs	• Cabinet • THASL • DDC
EARLY DETECTION	• Database of hepatitis and HCC • Lack of understanding among policy makers especially on HCC surveillance (surveillance = curative / no surveillance = death)	10	• More focus on high-risk groups such as cirrhosis patients for surveillance programs • Develop database	• *Department of medical services*
DIAGNOSIS / SURVEILLANCE	• GAAD cannot be reimbursed • Diagnosis options	10	• Surveillance should be reimbursed (Prevention + Promotion)	• Department of medical services • THASL • Service plan
ACCESS TO TREATMENT	• RFA for early stage cannot be reimbursed In UHC • Systemic therapy cannot be reimbursed	10	• Improve benefits in UHC • Ablation needles should be reimbursed in UHC scheme • Consider systemic therapies in down stage of HCC patients for UHC	• NLEM • NHSO + SSO

Vietnam (1/2)

PATIENT JOURNEY STAGE	CHALLENGE	HOW CRITICAL IS IT TO ADDRESS THIS CHALLENGE? [*on a scale of 10*]	POTENTIAL SOLUTION(S)	RESPONSIBLE AGENCY / DEPARTMENT
AWARENESS	• Lack of community awareness, compared to the level of awareness of lung cancer and breast cancer • Under estimate the risk of HCC • Disparity in awareness between urban and rural areas	• 10	• Build community awareness by tailored approach to different target population/ groups (social media, primary healthcare centers, lowest community level like ward)	• MOH • Provincial health department • Commune health department • Patient associations
PREVENTION	• HCV is not under National Immunization Program (NIP) • HBV is under NIP but some outreach community have not accessed to this yet • HBV/HCV test have not yet considered as universal test	• 7	• Develop policy on HCC prevention, including vaccination and HBV/HCV est • Call for funding from organisations	• CDC under MOH • Pharma companies
EARLY DETECTION	• Screening is not covered by National Health Insurance (NHI) • Lack of screening guidelines • Lack of healthcare workforce and infrastructure for screening (technology, classification of High-Low risk groups)	• 10	• Research on cost effectiveness of screening programs • Develop screening guidelines for recommendation • Capacity building for healthcare workforce	• MOH • VN cancer associations • National cancer hospitals

Vietnam (2/2)

PATIENT JOURNEY STAGE	CHALLENGE	HOW CRITICAL IS IT TO ADDRESS THIS CHALLENGE? [*on a scale of 10*]	POTENTIAL SOLUTION(S)	RESPONSIBLE AGENCY / DEPARTMENT
DIAGNOSIS	• Challenge in having accurate and timely diagnostics (unbalance workforce, diagnostics technology and tools, access to diagnostics	• 9	• Capacity/ capability building on diagnostics expertise (ultra sound/ CT/ MRI) • Provide free test/ diagnostics	• MOH • VN cancer associations • National cancer hospitals
ACCESS TO TREATMENT	• Lack of advanced medicine / therapy (regulatory, insurance coverage) • Limited access to HCC treatment centers (especially severe or late stage cancer to be treated in big hospitals only) • Lack of specialists/ treatment centers in provincial hospitals	• 8	• HCC treatment guidelines to be updated more frequently • Increase % of subsidy and increase access to lower level of hospitals (provincial) • Capacity/ capability building for healthcare workforcw	• MOH • Associations • PAP/PSP from pharma companies

APAC Hepatocellular Carcinoma Policy Forum 2024

Bangkok October 2, 2024

The APAC HCC Policy Forum is hosted by the APAC Liver Disease Alliance which is supported by AstraZeneca and Roche.

Closing Remarks

Roberta Sarno
APAC Liver Disease Alliance

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Co-Hosts:

กรมการแพทย์
Department of Medical Services

สถาบันมะเร็งแห่งชาติ
National Cancer Institute

一般社団法人 日本肝臓学会
The Japan Society of Hepatology

Supporting Today's Event:

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Summary of key discussions

1. **Importance of multistakeholder collaboration**
2. **Best practices in HCC surveillance and management**
3. **Policy recommendations and roadmap for improving patient outcomes**

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Next Steps

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Next Steps:

1. The APAC Liver Disease Alliance will share with participants the slides presented during the Forum, the outcomes of the workshop (i.e., the country roadmaps), and a summary of the event.

2. The APAC Liver Disease Alliance will also initiate the process of consolidating the workshop roadmap into a policy paper, inviting participants to co-author the paper and involve them throughout the process.

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Thank you!

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