

Hepatitis B : Australian Progress and Challenges

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www.doherty.edu.au/whoccvh



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Declaration of Interest

I receive no funding of any kind – research funding, speaking fees, honoraria, in-kind support, or any other form of remuneration - from any pharmaceutical or other for-profit health-care-related company

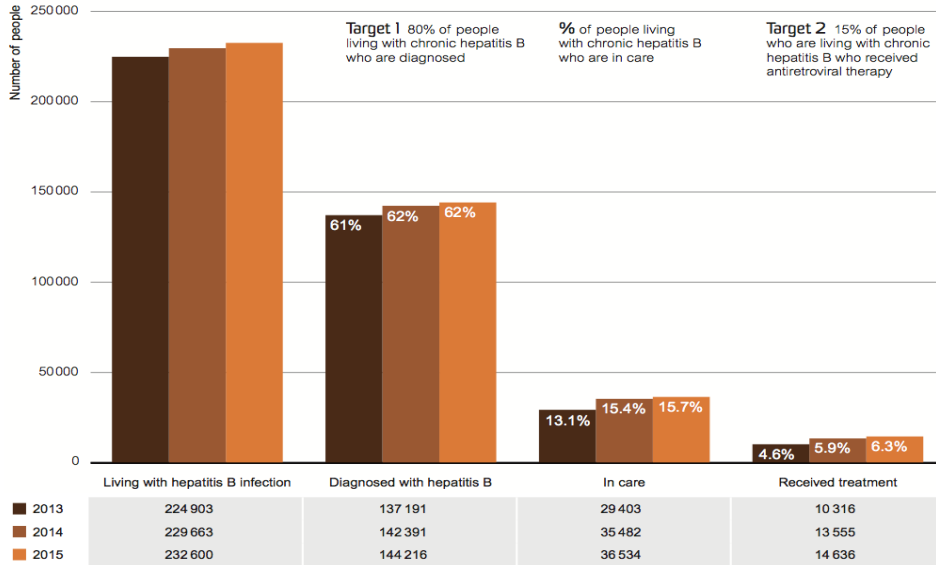
Advisory

For people living with viral hepatitis



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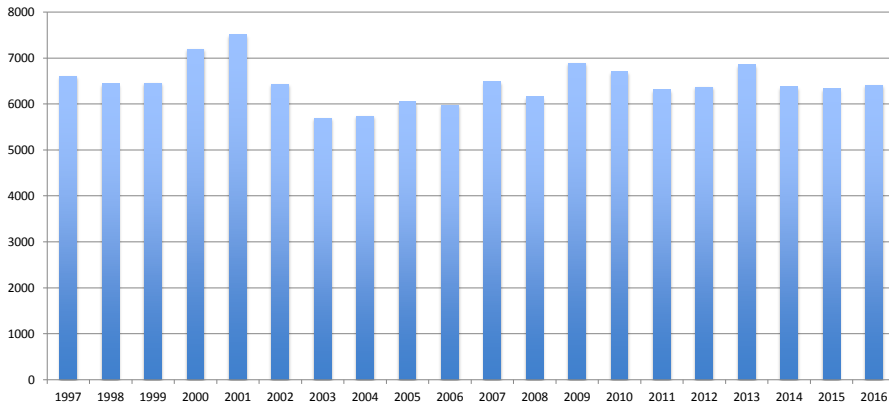
Australian progress?



Note: Due to updated modelling methods, estimates may be different to figures presented in previous years of reporting
 Source: WHO Collaborating Centre for Viral Hepatitis, Victorian Infectious Diseases Reference Laboratory, Doherty Institute

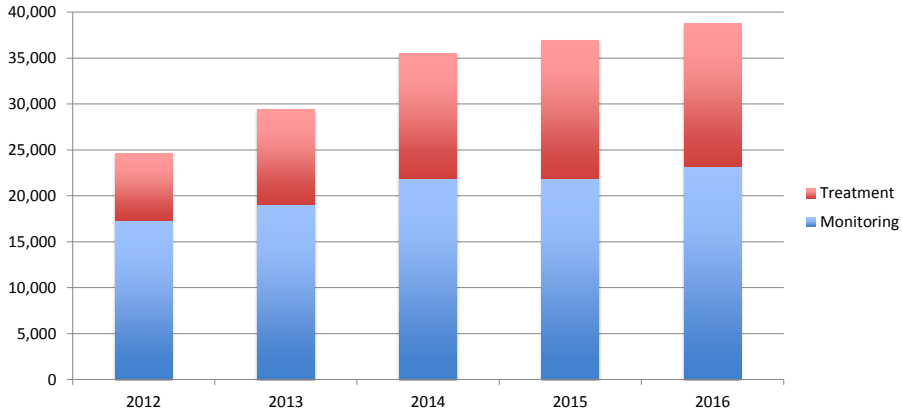
Diagnosing >6000 people per year

Number of notifications for unspecified HBV, 1997-2016

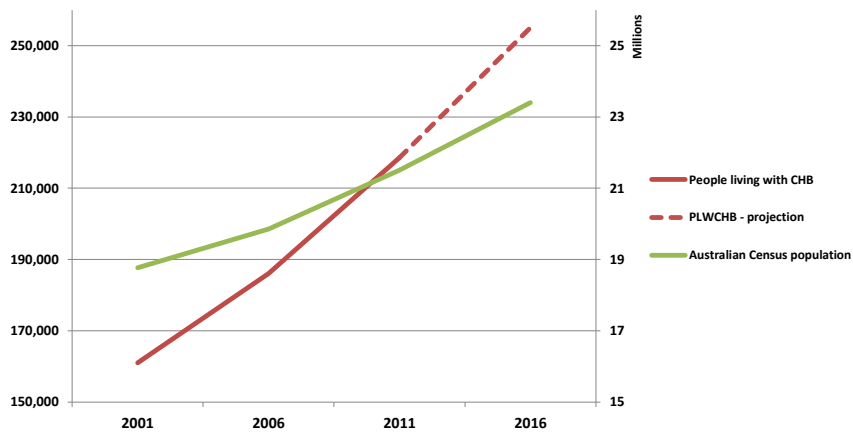


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Several thousand more people in care every year. . .



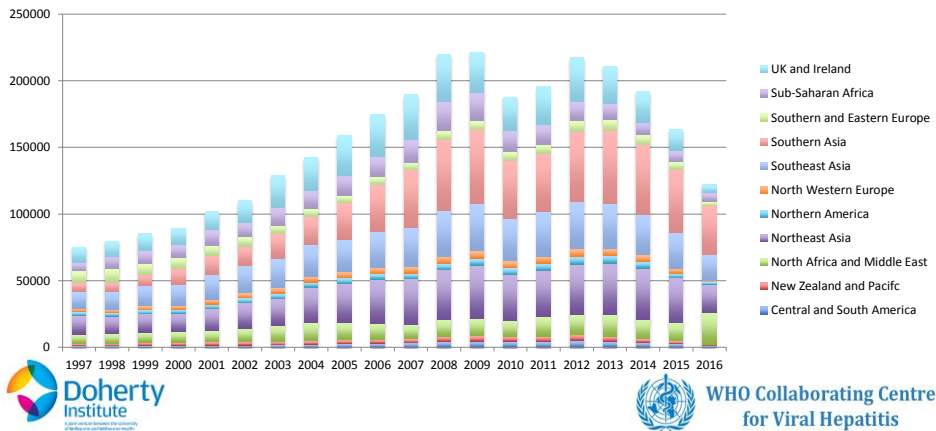
Census-based estimates of PLWCHB in Australia



Estimating prevalence

Indicators of care remain stable due to migration of people living with CHB to Australia

Permanent arrivals by world region, 1997-2016



Oral Abstracts - Concurrent 3: Understanding the Epidemics

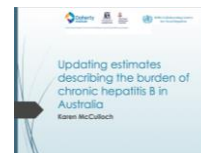
Karen McCulloch - Updating Estimates Describing the Burden of Hepatitis B in Australia*

Thursday, August 10, 2017

3:20 PM - 3:30 PM

Tully Room I

(*Conflict of Interest)

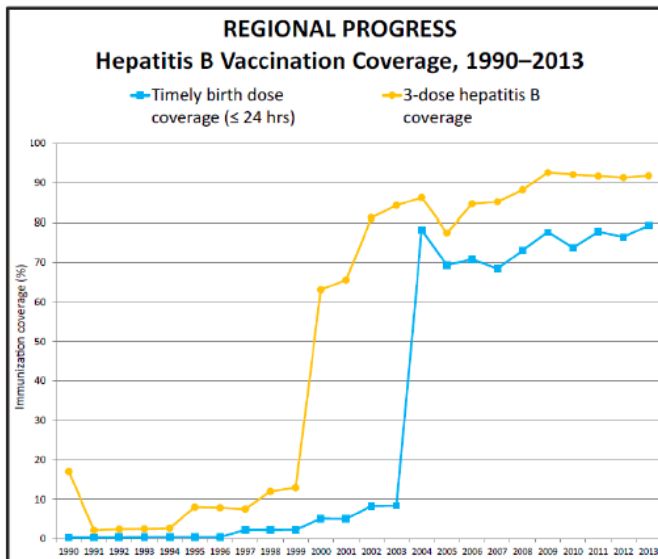


Overestimating the burden of CHB in Australia. . .

. . . for good reasons?



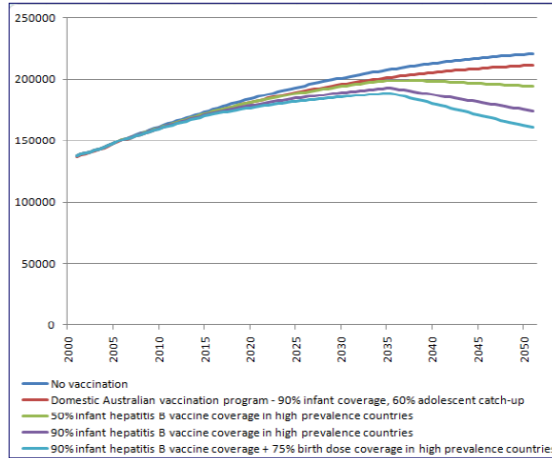
Vaccination Coverage



Source: WHO/UNICEF Joint Reporting Form (JRF) for Immunization

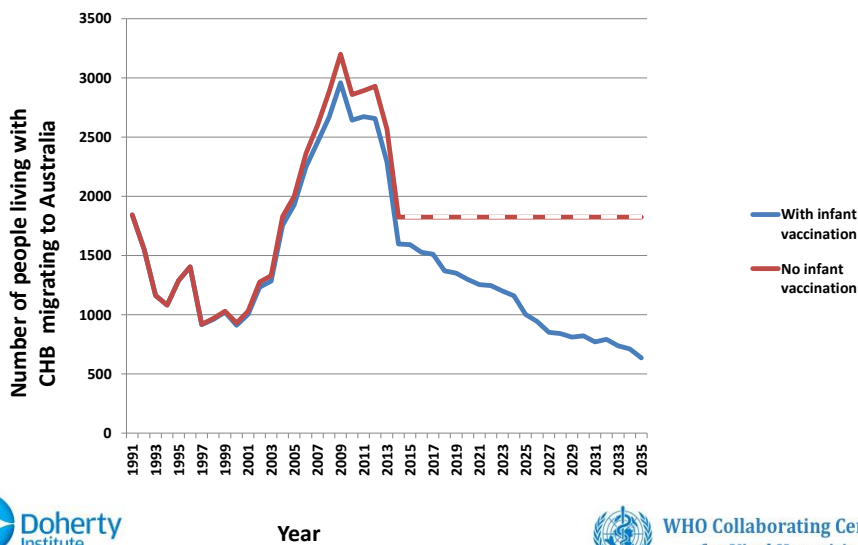


How supporting infant hepatitis B vaccination overseas helps Australia



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Effect of current vaccination programs in China, Vietnam and the Philippines on the future burden of CHB in Australia



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“The People’s Vaccine” - Blumberg

Vaccine 27 (2009) 6550–6557

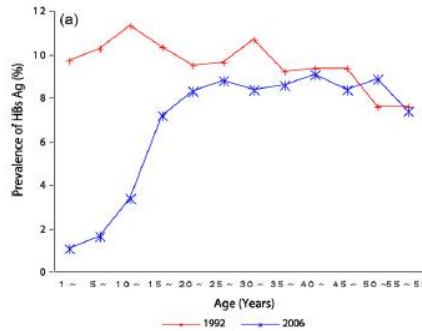


Epidemiological serosurvey of Hepatitis B in China—Declining HBV prevalence due to Hepatitis B vaccination^a

Xiaofeng Liang^a, Shengli Bi^b, Weizhong Yang^a, Longde Wang^a, Gang Cui^c, Fuqiang Cui^a, Yong Zhang^b, Jianhua Liu^a, Xiaohong Gong^a, Yuansheng Chen^a, Fuzhen Wang^a, Hui Zheng^a, Feng Wang^b, Jing Guo^c, Zhiyuan Jia^b, Jingchen Ma^d, Huaqing Wang^a, Huiming Luo^e, Li Li^f, Shuigao Jin^a, Stephen C. Hadler^g, Yu Wang^{h,i}

^a Chinese Center for Disease Control and Prevention, Beijing, China
^b Institute of Virology Disease Control, Chinese Center for Disease Control and Prevention, Beijing, China
^c Ministry of Health, China
^d Fujian Provincial Center for Disease Control and Prevention, China
^e WHO Representative Office in China, China

- 5yo: <1% CHB
- China: 7.2%
- >35 million chronic infections averted
- >5 million future deaths prevented



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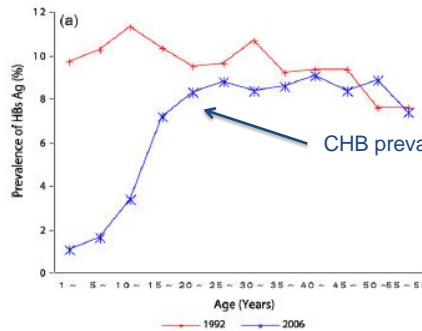


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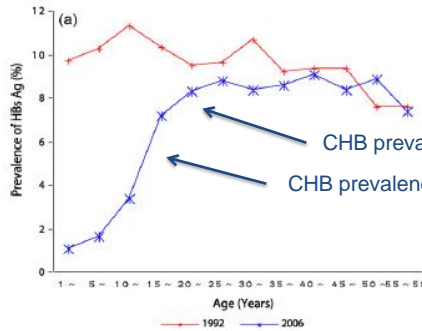


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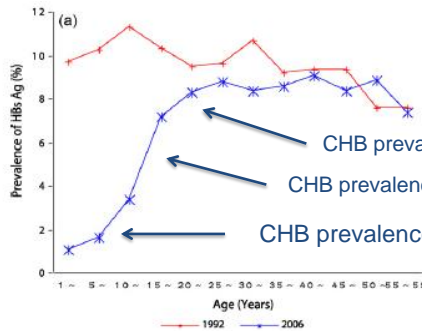


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Overestimating the burden of CHB in Australia. . .

. . . for bad reasons?

Since around 2014, increasing cases of people applying for permanent residency in Australia being denied on the grounds of having hepatitis B.

- with thanks to Lachlan Riches, Taylor and Scott Lawyers and Migration Institute of Australia



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Migration Regulations 1994 - legalised discrimination

- Schedule 4 Regulations (Public Interest Criteria-PIC)
- HEALTH PIC'S 4005, 4006A AND 4007
- *"is free from tuberculosis; and*
- *is free from a disease or condition that is, or may result in the applicant being, a threat to public health in Australia or a danger to the Australian community; and*
- *.... is free from a disease or condition in relation to which a person who has it would be likely to require health care or community services during the period [OF THE VISA APPLIED FOR]; and...*



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HEALTH PIC'S

- *....the provision of the health care or community services would be likely to... result in a **significant cost** to the Australian community in the areas of health care and community services - regardless of whether the health care or community services will actually be used in connection with the applicant*
- *Medical Officers of the Commonwealth (MOCs) must provide an opinion as to whether an applicant's condition or disease would be likely to result in 'significant' health care and community service costs if a visa were to be granted.... The policy threshold for the level of costs regarded as significant is currently \$ 40,000.*



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Australia's migration health requirements and discrimination

DISABILITY DISCRIMINATION ACT 1992 (Cwth.)

s.4....."disability " , in relation to a person, means:....

- *(c) the presence in the body of organisms causing disease or illness; or*
- *(d) the presence in the body of organisms capable of causing disease or illness..."*

Thus living with viral hepatitis is accepted as a disability

Australia has always asserted the right to 'exempt' its migration law and policies regime from domestic and international prohibitions against discrimination



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Australia's 'interpretive declaration' on ratification of Convention

“Australia recognizes the rights of persons with disability to liberty of movement, to freedom to choose their residence and to a nationality, on an equal basis with others.

Australia further declares its understanding that the Convention does not create a right for a person to enter or remain in a country of which he or she is not a national, nor impact on Australia's health requirements for non-nationals seeking to enter or remain in Australia, where these requirements are based on legitimate, objective and reasonable criteria.”



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HEALTH 'WAIVERS' PIC 4006A/4007

- PIC 4007: “The Minister may waive the requirements of paragraph (1)(c) if
 - the applicant satisfies all other criteria for the grant of the visa applied for; and
 - the Minister is satisfied that the granting of the visa would be unlikely to result in:
 - **undue cost** to the Australian community; or
 - **undue prejudice to the access** to health care or community services of an Australian citizen or permanent resident.”



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RACGP Red Book



- The Red Book is now widely accepted as the main guide to the provision of preventive care in Australian general practice. It covers primary (preventing the initial occurrence of a disorder) and secondary (preventive early detection and intervention) activities.
- Hepatitis B:
 - STI check
 - Antenatal screening
 - Immunisation



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The impact of late diagnosis - BC

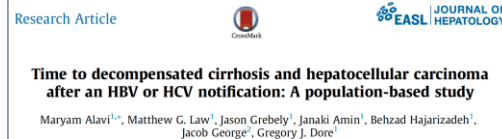


- Late diagnosis (within 2 years prior, or after)
 - Decompensated cirrhosis
HBV: 49% HCV: 40%
 - Liver cancer
HBV: 46% HCV: 31%
- HBV late diagnosis
 - Declined from 100% in 1992 to 11%/26% in 2011
 - Associated with mental illness, and fewer medical visits in the 5 years prior



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The impact of late diagnosis - NSW



- Late diagnosis (within 2 years prior, or after)
 - Decompensated cirrhosis
HBV: 43% HCV: 29%
 - Liver cancer
HBV: 38% HCV: 22%
- HBV late diagnosis
 - Declined from 64/68% in 2001 to 31/29% in 2011



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Access to timely diagnosis and care – human rights basis

United Nations Convention on the Rights of Persons with Disabilities

Article 25 - Health

States recognize that persons with disabilities have the right to the enjoyment of the highest attainable standard of health without discrimination on the basis of disability. States will;

- Provide persons with disabilities with the same range, quality and standard of free or affordable health care and programmes as provided to other persons, including in the area of sexual and reproductive health and population-based public health programmes;
- Provide those health services needed by persons with disabilities specifically because of their disabilities, including early identification and intervention as appropriate, and services designed to minimize and prevent further disabilities
- Provide these health services as close as possible to people's own communities, including in rural areas



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Access to timely diagnosis and care – legal basis

- Failure to diagnose hepatitis B in a person with identifiable risk factors, leading to a poor outcome for the individual, could create a situation in which a doctor has breached their duty of care
- Recommendations (since at least the early 1990s) then clinical guidelines – and more recently national testing policies – state that people born overseas, and Aboriginal and Torres Strait Islander people (among others) should be offered testing for hepatitis B
- Cases in the USA of liver cancer caused by undiagnosed HBV – all settled out of court so far? → Australia and other countries?

Opportunity to reframe the testing question – away from responsibilities, and towards RIGHTS



Mapping progress in chronic hepatitis B: geographic variation in prevalence, diagnosis, monitoring and treatment, 2013–15

Jennifer MacLachlan,^{1,2} Nicole Allard,^{1,2} Kylie Carville,^{1,2} Kaitlin Haynes,^{1,2} Benjamin Cowie^{1,2}
 2017 Ozone Australian and New Zealand Journal of Public Health

United Nations Convention on the Rights of Persons with Disabilities Article 25 - Health

States will provide these health services as close as possible to people's own communities, including in rural areas



Figure 2: Heat map of CHB burden and access to care by Primary Health Network, ranked by CHB prevalence, 2014.

State/Territory	Primary Health Network	BURDEN OF CHRONIC HEPATITIS B		TREATMENT AND MONITORING UPTAKE	
		Prevalence	Diagnosis	Treatment	Care
		Proportion of the population living with CHB	CHB notification rate per 100,000	Proportion of people receiving CHB treatment	Proportion of people receiving CHB treatment or monitoring
NT	Northern Territory	1.77%	61.6	3.1%	17.0%
NSW	South Western Sydney	1.61%	41.1	13.7%	31.2%
NSW	Western Sydney	1.55%	64.8	10.0%	23.3%
NSW	Central and Eastern Sydney	1.44%	52.3	8.8%	22.8%
VIC	North Western Melbourne	1.35%	48.1	6.8%	21.4%
QLD	Western Queensland	1.19%	26.9	0.8%	1.8%
VIC	Eastern Melbourne	1.14%	32.7	7.6%	23.0%
NSW	Northern Sydney	1.11%	46.7	9.9%	26.2%
VIC	South Eastern Melbourne	1.10%	23.9	6.4%	19.8%
QLD	Brisbane South	1.09%	37.7	5.4%	12.9%
ACT	Australian Capital Territory	1.01%	24.7	5.5%	14.7%
SA	Adelaide	0.99%	22.5	4.2%	6.2%
WA	Perth North	0.98%	25.9	4.4%	7.5%
WA	Perth South	0.96%	26.4	3.5%	6.4%
QLD	Northern Queensland	0.95%	16.6	1.6%	4.3%
WA	Country WA	0.92%	18.3	1.0%	3.0%
NSW	Western NSW	0.84%	15.7	1.3%	3.9%
QLD	Brisbane North	0.76%	18.2	2.5%	5.1%
QLD	Darling Downs and West Moreton	0.73%	9.6	2.3%	5.3%
NSW	Nepean Blue Mountains	0.73%	6.1	3.0%	7.0%
QLD	Gold Coast	0.71%	14.1	3.4%	6.5%
NSW	South Eastern NSW	0.71%	8.9	2.4%	6.5%
TAS	Tasmania	0.68%	10.7	1.4%	3.4%
NSW	Murrumbidgee	0.66%	16.7	1.8%	5.0%
NSW	Hunter New England and Central Coast	0.66%	8.8	2.0%	5.4%
NSW	North Coast	0.66%	7.5	1.9%	5.2%
QLD	Central Queensland and Sunshine Coast	0.63%	7.0	1.5%	3.0%
SA	Country SA	0.63%	10.9	1.2%	1.9%
VIC	Murray	0.61%	8.9	2.6%	7.9%
VIC	Gippsland	0.57%	6.0	2.1%	5.5%
VIC	Grampians and Barwon South West	0.56%	8.1	1.6%	6.9%



The geographic disparities in access to treatment and care across Australia reveal the underlying, pervasive and urgent health inequity in this country

News of the tragic death of Dr G. Yunupingu last week in Darwin at only 46 years of age has again highlighted the unacceptable gap in life expectancy between Aboriginal and Torres Strait Islanders and other Australians. Yunupingu had been [living with chronic hepatitis B](#) since early in life, and experienced complications of this condition including liver and kidney disease.

Oral Abstracts - Concurrent 3: Understanding the Epidemics

Kelly Hosking - Tracking In Arnhem Land – On the Hunt for Hepatitis B Virus

Thursday, August 10, 2017

3:00 PM – 3:15 PM

Tully Room I



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From Treatment – to Cure?



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www.hepb.org/treatment-and-management/drug-watch/

FAMILY/DRUG NAME	MECHANISM	COMPANY	WEBSITE	USA STATUS	FAMILY/DRUG NAME	MECHANISM	COMPANY	WEBSITE	USA STATUS
Silencing RNA's (siRNAs): Interferes and destroys viral RNA					Antisense Molecules: Binds to the viral mRNA to prevent it from turning into viral protein				
ARB-1467	RNAi gene silencer (1.0)	Arbutus Biopharma, Canada	arbutusbio.com	Phase II	IONIS-HBVRx (GSK3228836)	Viral protein inhibitor	Ionis Pharma, USA with GSK	ionispharma.com	Phase I
ARB-1740	RNAi gene silencer (2.0)	Arbutus Biopharma	arbutusbio.com	Phase II	IONIS-HBVLrx (GSK3318242)	Viral protein inhibitor	Ionis Pharma with GSK	ionispharma.com	Phase I
RG6004 (HBV LNA)	RNA targeted via Locked Nucleic Acid	Roche	roche.com	Phase I/II	Ribonuclease H Inhibitors: Inhibit degradation of viral RNA				
ALN-HBV	RNAi gene silencer	Alnylam, USA	alnylam.com	Preclinical	RNaseH Inhibitor	Viral RNase inhibitor	Arbutus Biopharma, Canada	arbutusbio.com	Preclinical
Hepbarna (BB-HB-313)	RNAi gene silencer	Benitec, Australia	benitec.com	Preclinical	Therapeutic Vaccines: Vaccine technology used to stimulate the immune system as a treatment				
Lunar-HBV	RNAi gene silencer	Arcturus, USA with Janssen	arcturusrx.com	Preclinical	GS 4774	Therapeutic vaccine	Globetimmune, USA	globetimmune.com	Phase II
ARO-HBV	RNAi gene silencer	Arrowhead Pharma, USA	arrowheadpharma.com	Preclinical	INO-1800	Therapeutic vaccine	Inovio, USA	inovio.com	Phase I
Entry inhibitors: Interferes with HBV getting into liver cells					HB-110	Therapeutic vaccine	Ichor Medical Systems with Janssen, USA	ichorms.com	Phase I
Myrciludex B	Entry inhibitor	Hepatera, Russia with MYR GmbH, Germany	myr-pharma.com	Phase II	TG1050	Therapeutic vaccine	Transgene, France	transgene.com	Phase I
Capsid inhibitors: Interferes with the viral DNA protein shield					HepTcell	Therapeutic vaccine	Altimmune, USA	altimmune.com	Phase I
Morphothalidin (GL54)	Capsid inhibitor	HEC Pharma, PR China	pharm.hec.cn/en	Phase II	Tomegavax HBV	Therapeutic vaccine	Tomegavax, USA	tomegavax.com	Preclinical
NVR 3-778	Capsid inhibitor	Janssen, USA	janssen.com	Phase II	Innate Immune Defense Pathway: Compounds that activate the innate immune system				
AIC 649	Capsid inhibitor	AlCuris, Germany	alcuris.com	Phase I	GS 9620	TLR-7 agonist	Gilead Sciences	gilead.com	Phase II
JNJ56136379	Capsid inhibitor	Janssen, USA	janssen.com	Phase I	RO6864018 (RG7795, ANA773)	TLR-7 agonist	Roche	roche.com	Phase II
ABI-H0731	Capsid inhibitor	Assembly Biosciences, USA	assemblybio.com	Phase I	S89200	RIG -1 and NOD2 agonist	Spring Bank Pharmaceuticals, USA	springbankpharm.com	Phase II
AB-423	Capsid inhibitor	Arbutus Biopharma, Canada	arbutusbio.com	Phase I	GS9688	TLR-8 agonist	Gilead Sciences	gilead.com	Phase I
HBsAg inhibitors: Interferes with production of HBV surface antigen (sAg)					Host Acting Pathway: Compounds that induce programmed cell death (apoptosis)				
REP 2139	sAg inhibitor	Replicor, Canada	replicor.com	Phase II	EY001	FXR agonist	Enyo Pharma, France	enyopharma.com	Phase I
REP 2165	sAg inhibitor	Replicor, Canada	replicor.com	Phase II	CRV 431 (CPI 431-42)	Ciclofilin inhibitor	ContraVir, USA	contravir.com	Preclinical
					Other				
					GC1102	sAg monoclonal antibody	Green Cross, South Korea	www.globalgrencross.com	Phase II

We need to prepare for HBV cure

- Don't repeat the mistakes / time to scale up in HIV or HCV
- WHO / UNITAID / Global fund(s) / countries – prepare for pooled procurement, patent instruments, essential medicines listing updates NOW
- This applies to high income countries as well
 - Why did Germany pay 66,000 EUR per course of DAAs in 2015 and Australia pay 6,000 EUR per course of DAAs in 2016?
- HBV elimination modelling for WHO – estimated cure available from 2025
- Implementation & roll out – will require pre-existing diagnosis, care enrolment – established by diagnosing and treating eligible people with CHB NOW
- Added benefit – save more than half a million lives/year while we wait



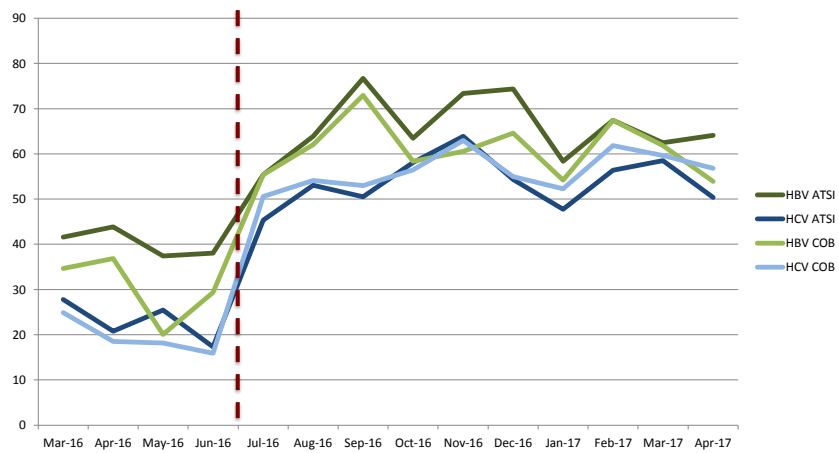
Negotiating better discounts for DAA therapy is critical to achieve HCV elimination by 2030

Gregory J. Dore, Jason Grebely
The Kirby Institute, UNSW Sydney, Sydney, Australia

Investment - workforce

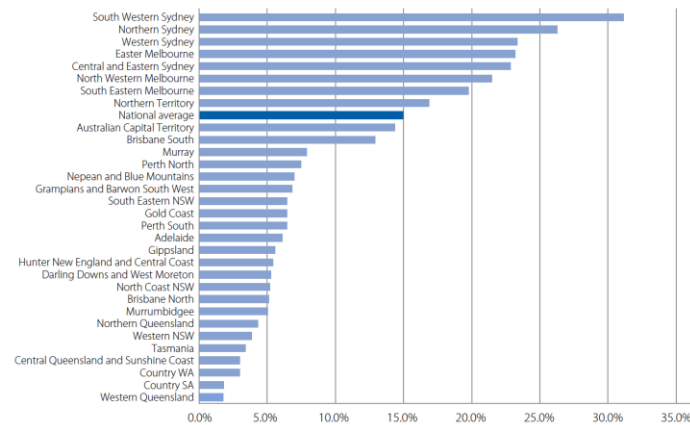


Victorian Viral Hepatitis Enhanced Surveillance Pilot



ENGAGEMENT IN CARE

Figure 7: Engagement in care by Primary Health Network, 2014 - proportion of people living with CHB who received treatment or monitoring



Data source: Department of Human Services Medicare statistics.



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Hepatitis B – progress and challenges

- The rest of Australia needs to chase Sydney SW – such gross inequities in access to care are unacceptable and appear to violate our human rights treaty obligations
- While we're doing that – Sydney SW needs to double those receiving care
- The national strategies revision process must be harnessed to achieve these objectives
- Yes – we should continue to seek parity with HIV and HCV responses
 - but instead of that perennial focus, making national equity in CHB responses must be an immediate and achievable goal



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Nicole Allard, Chelsea Brown, Kylie Carville,
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CRC-SI
Doherty Institute



www.doherty.edu.au/whoccvh



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