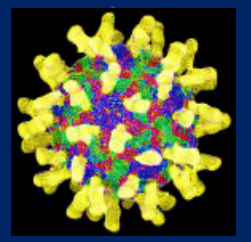
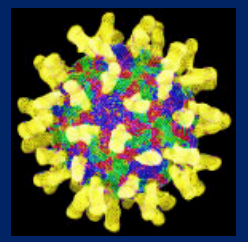
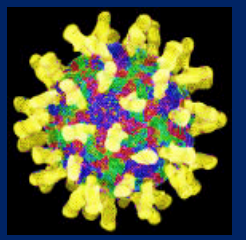
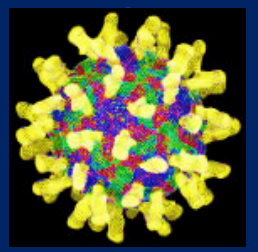








Moving Towards Hep C Elimination in NZ

Jacqui Stone NP

CADS
COMMUNITY
ALCOHOL & DRUG
SERVICES
Te Wai Awhina
Rongoatia O Tamaki

CADS South

Liver Clinics

All have access to Fibroscan/SWE, blood tests and treatment

- **Localities Hubs at Mangere, Botany and Manukau SuperClinic**
- **Liver Clinic at Middlemore Hospital**
  - ✓ Booked appointments via e-referrals
- **Walk-in clinic at CADS South**
  - ✓ Every 2nd Thursday each month (9am-3pm)
- **Prisons (Wiri Men's and Women's)**
  - ✓ Monthly (alternately) and have access to Fibroscan, treatment and blood tests.

Viral Hepatitis

5 types:

A: faecal-oral transmission

B: sexual fluids & blood to blood

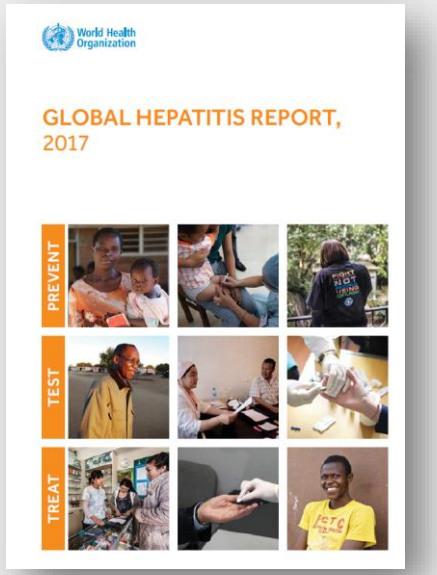
C: blood to blood

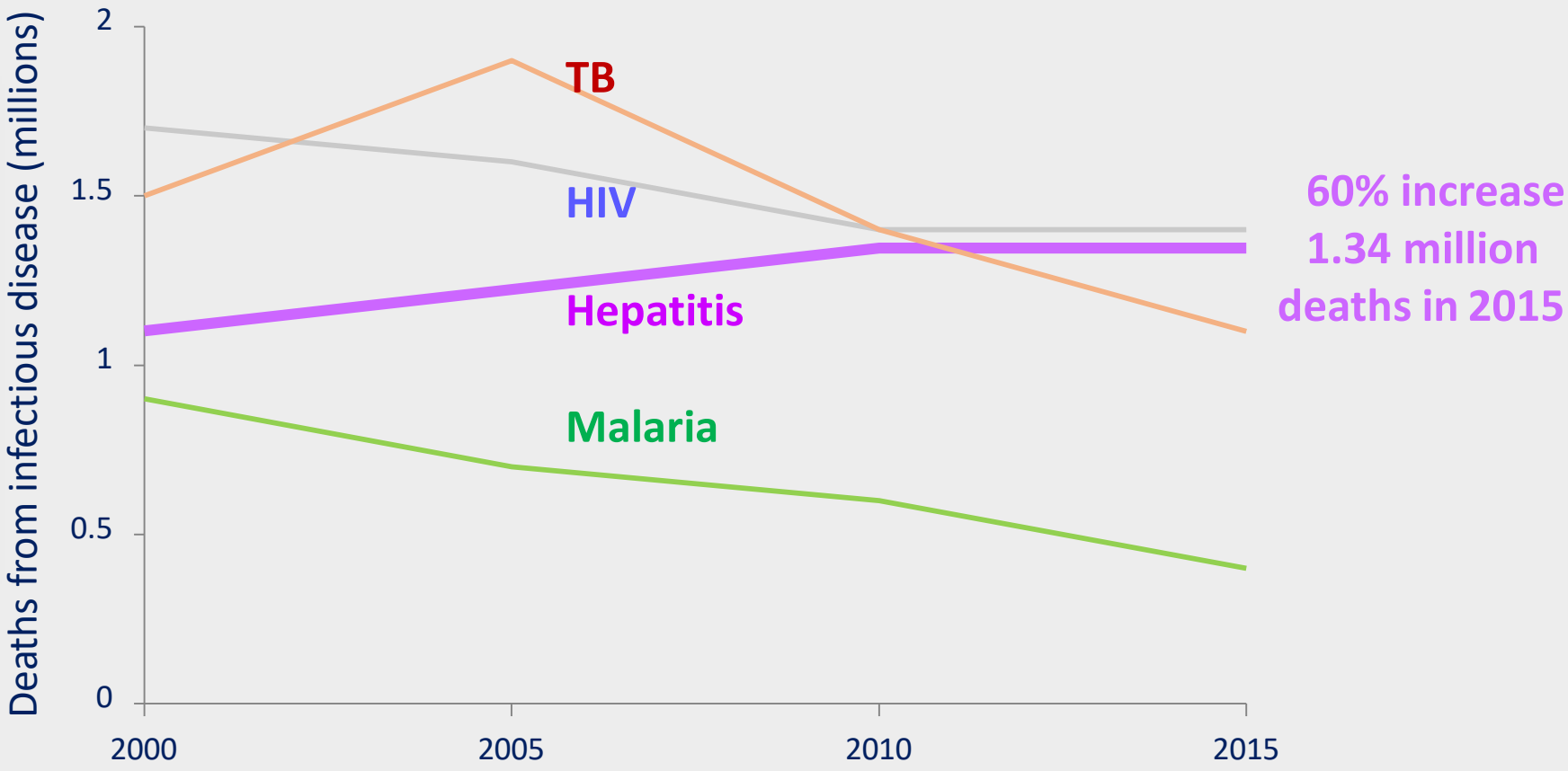
D: travels with B

E: faecal–oral transmission

Vaccine Preventable

Increasing Deaths from Viral Hepatitis

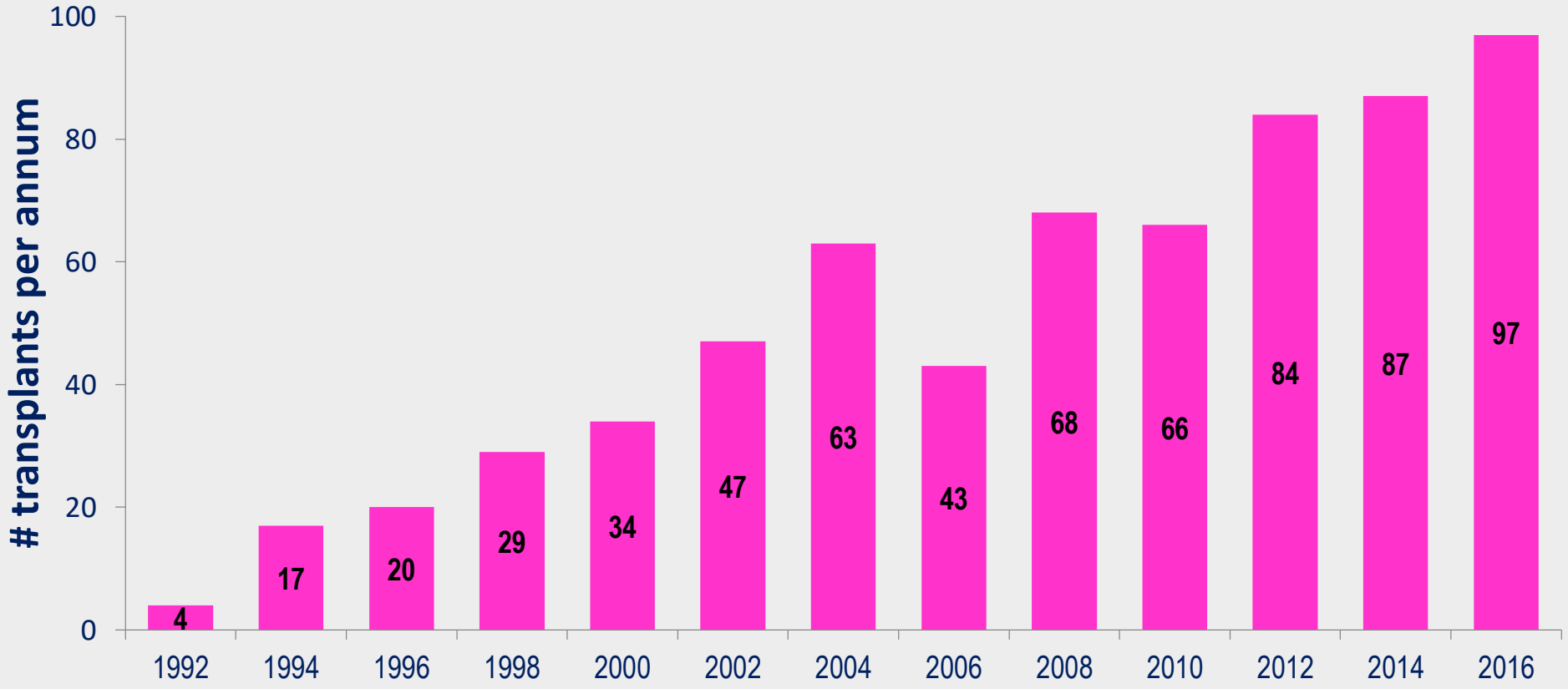




Global Burden of Disease 2013. Lancet 2015;385:117–71
WHO 2017 Global Hepatitis Report

Increasing HCV Disease Burden in New Zealand

(i) HCV-related Liver Transplants at ANZLTR



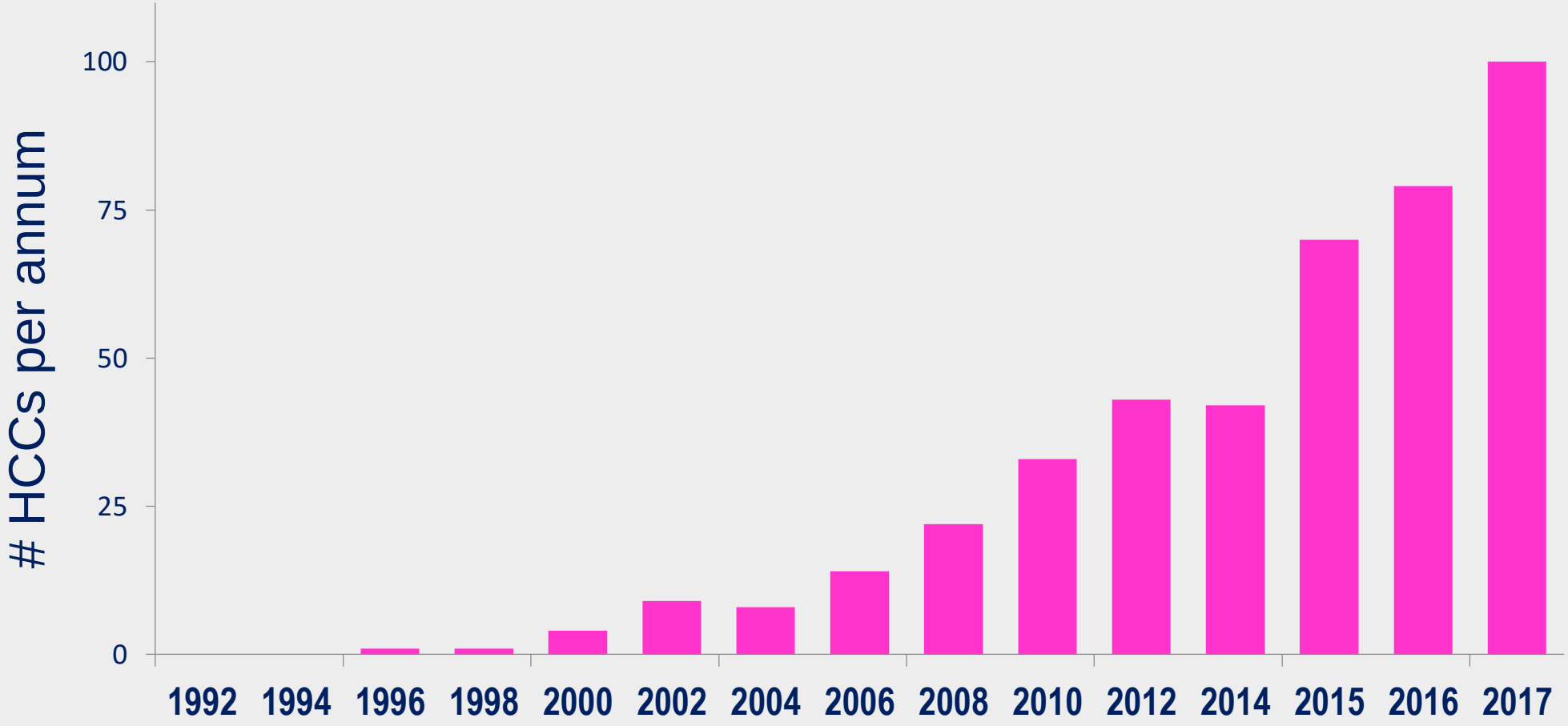
ANZLTR DATA TO 31/12/2016
SECTION 2 : Primary Diagnosis

28th Australian and New Zealand Liver Transplant Registry. Available at http://www.sswahs.nsw.gov.au/gastro/livertransplant/RPAH2011/

Hepatitis C
Get tested
Get cured!

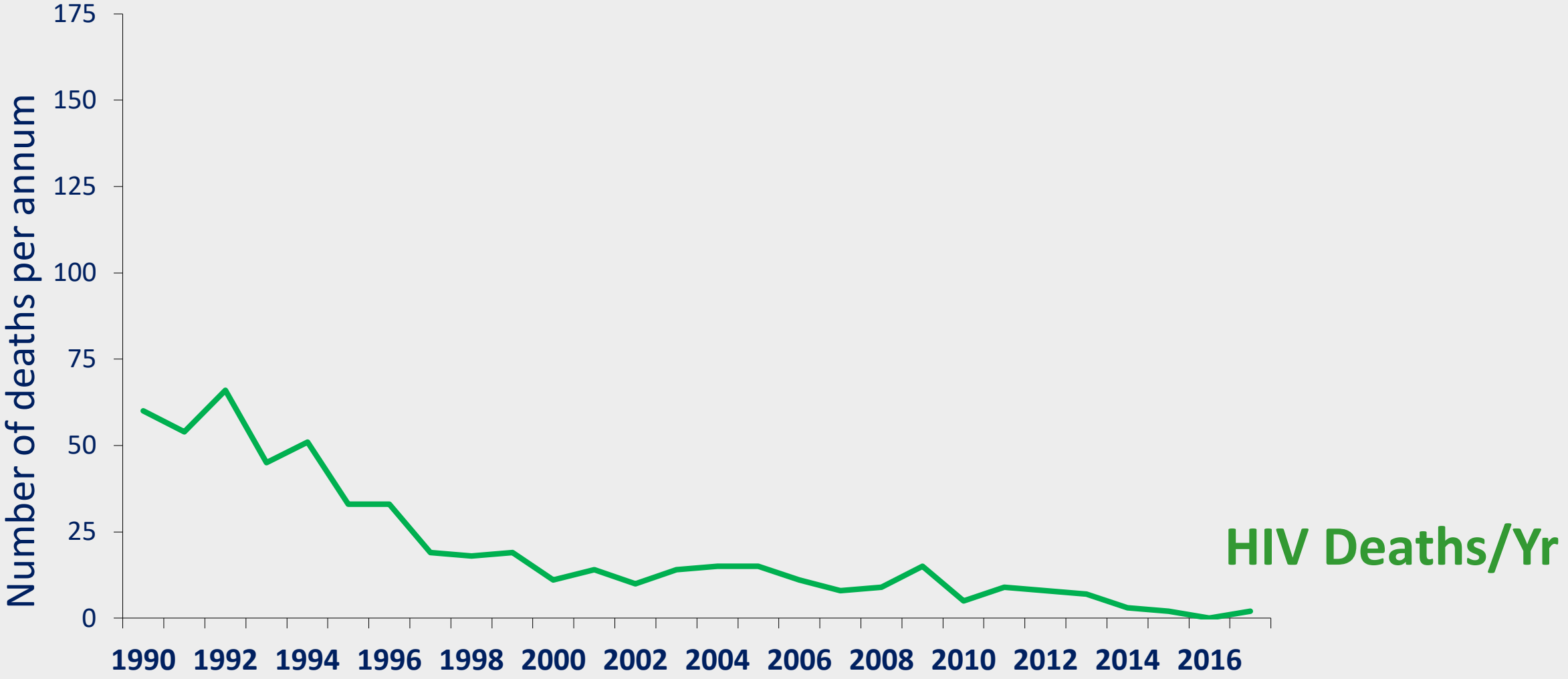
Increasing HCV Disease Burden in New Zealand

(ii) HCV-related Liver Cancer at Auckland Hospital



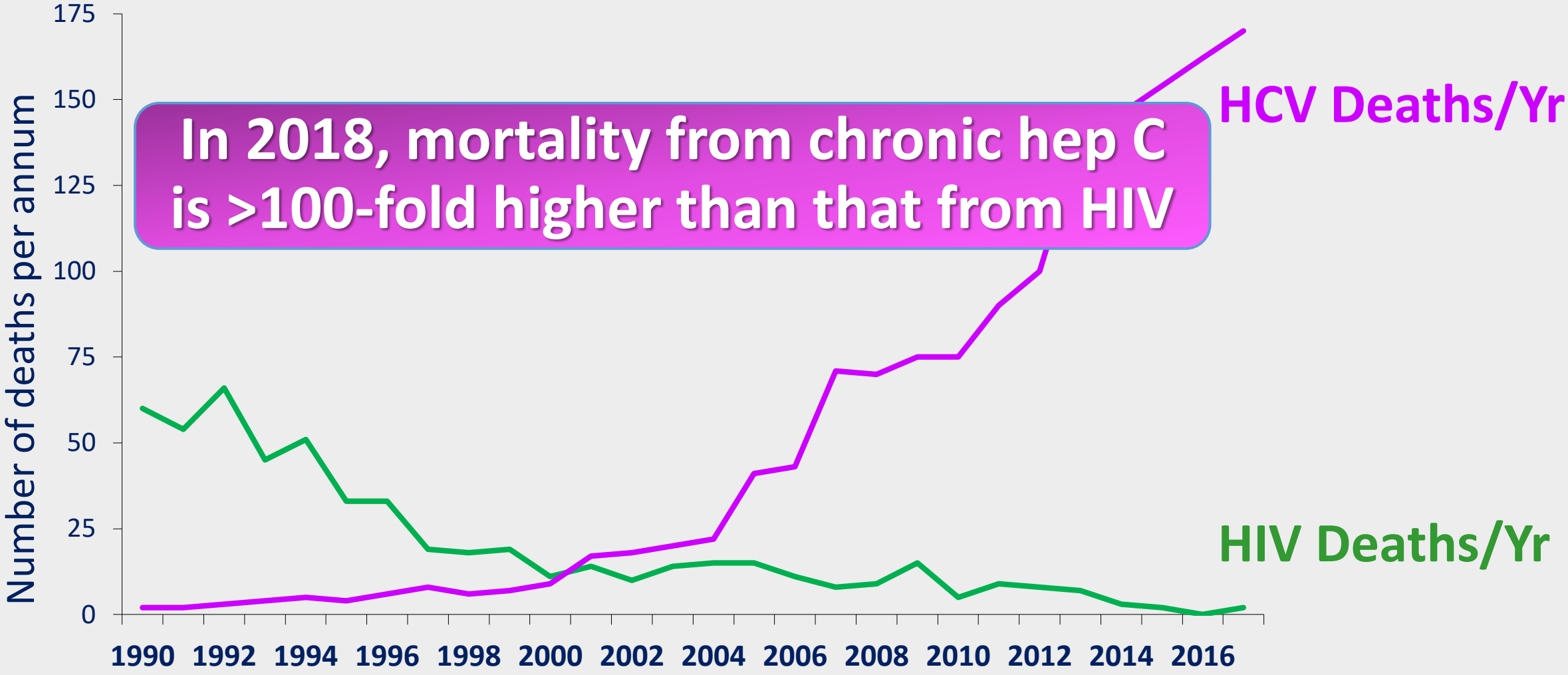
NZLTU HCC MDM data on file

Improved HIV Awareness, Testing & Treatment Have Resulted in Declining Mortality From AIDS



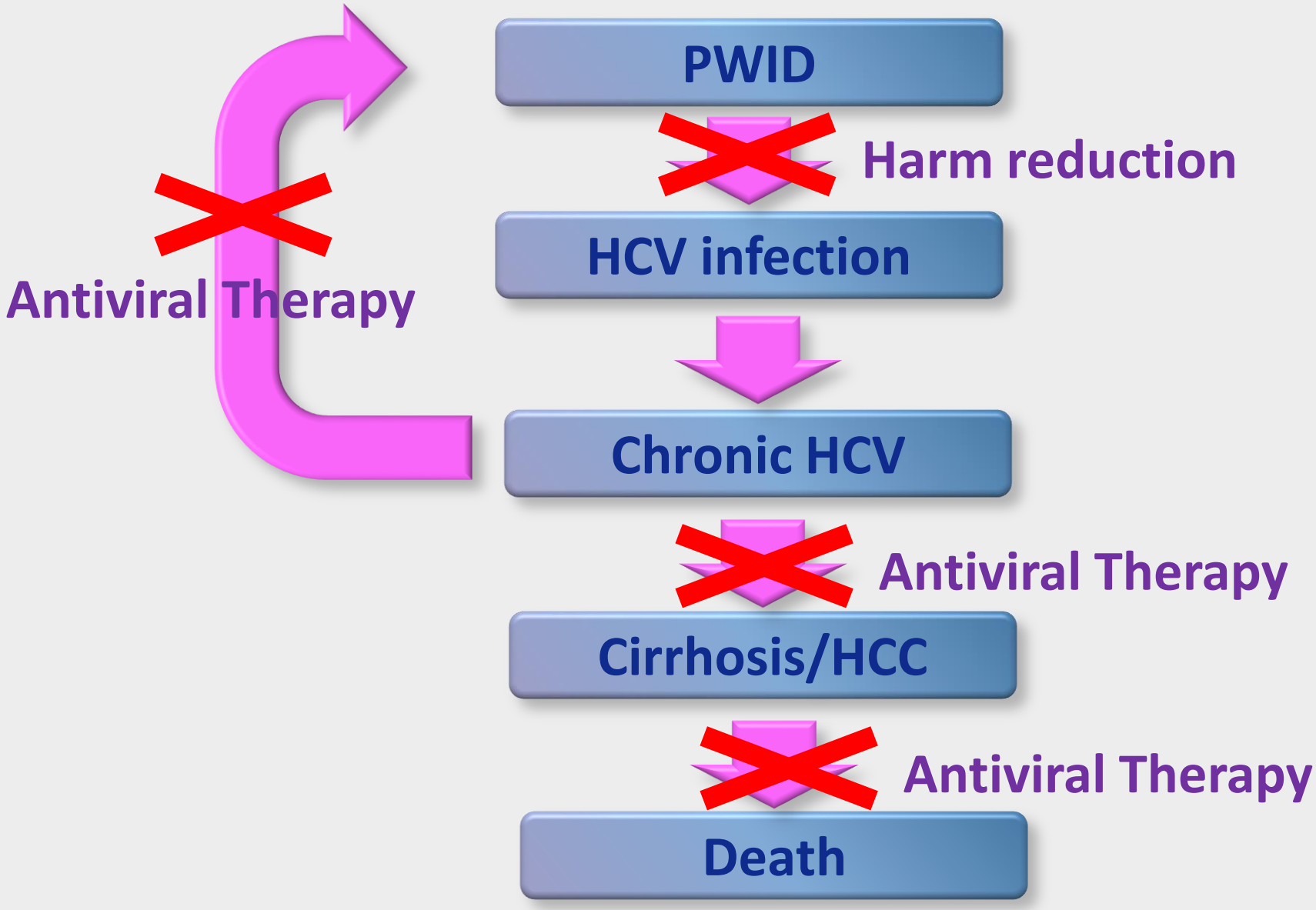
AIDS-New Zealand Issue 77 - June 2018; ISSN 1170-2656

Poor HBV & HCV Awareness, Testing & Treatment Have Resulted in Climbing Mortality from Hepatitis

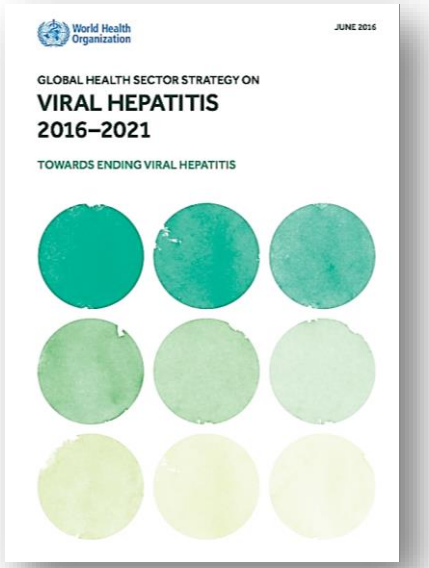


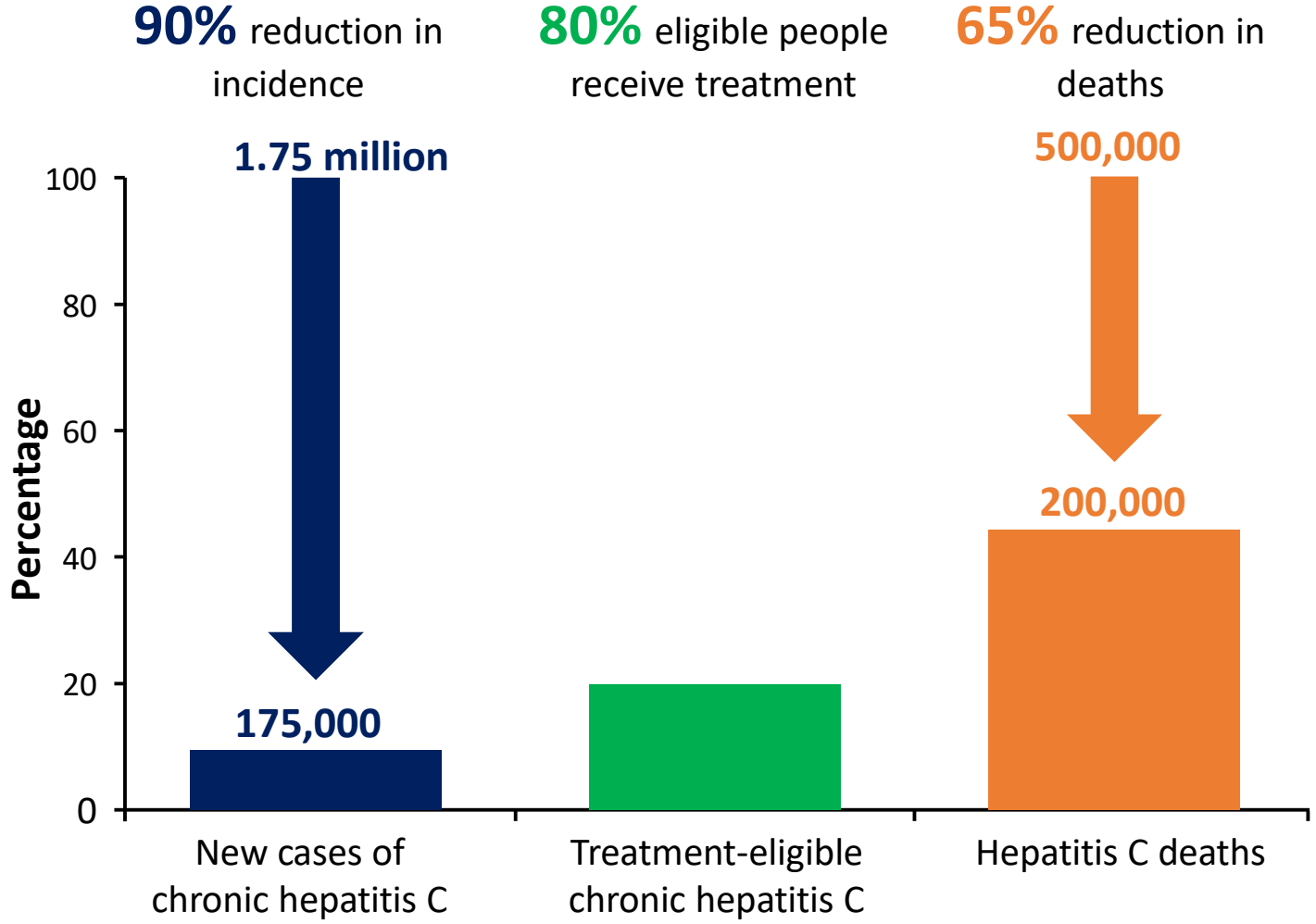
AIDS-New Zealand Issue 77 - June 2018; ISSN 1170-2656

How Can We Reduce HCV Infections and Deaths?



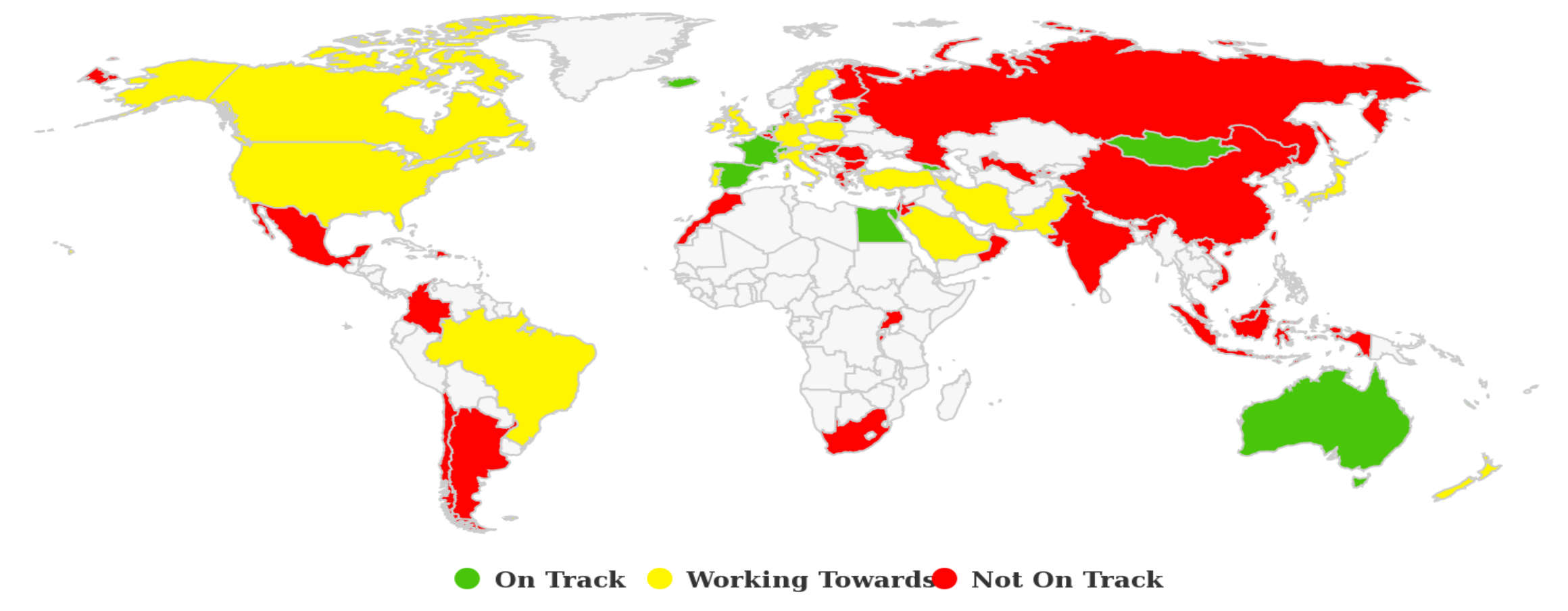
WHO has Set Ambitious Global Targets by 2030





WHO global health sector strategy on viral hepatitis. Available at: http://apps.who.int/iris/bitstream/10665/246177/1/WHO-HIV-2016.06-eng.pdf?ua=1 (accessed April 2017)

WHO HCV Elimination Targets: 2017



On-track (2016): Iceland, Qatar, Netherlands, Australia, France, Germany, Japan, Egypt, Georgia

On-track (2017): Iceland, Qatar, Netherlands, Australia, France, Germany, Japan, Egypt, Georgia, Spain, Switzerland, Mongolia

CDA 2018: Polaris Observatory (http://centerforda.com/polaris/)

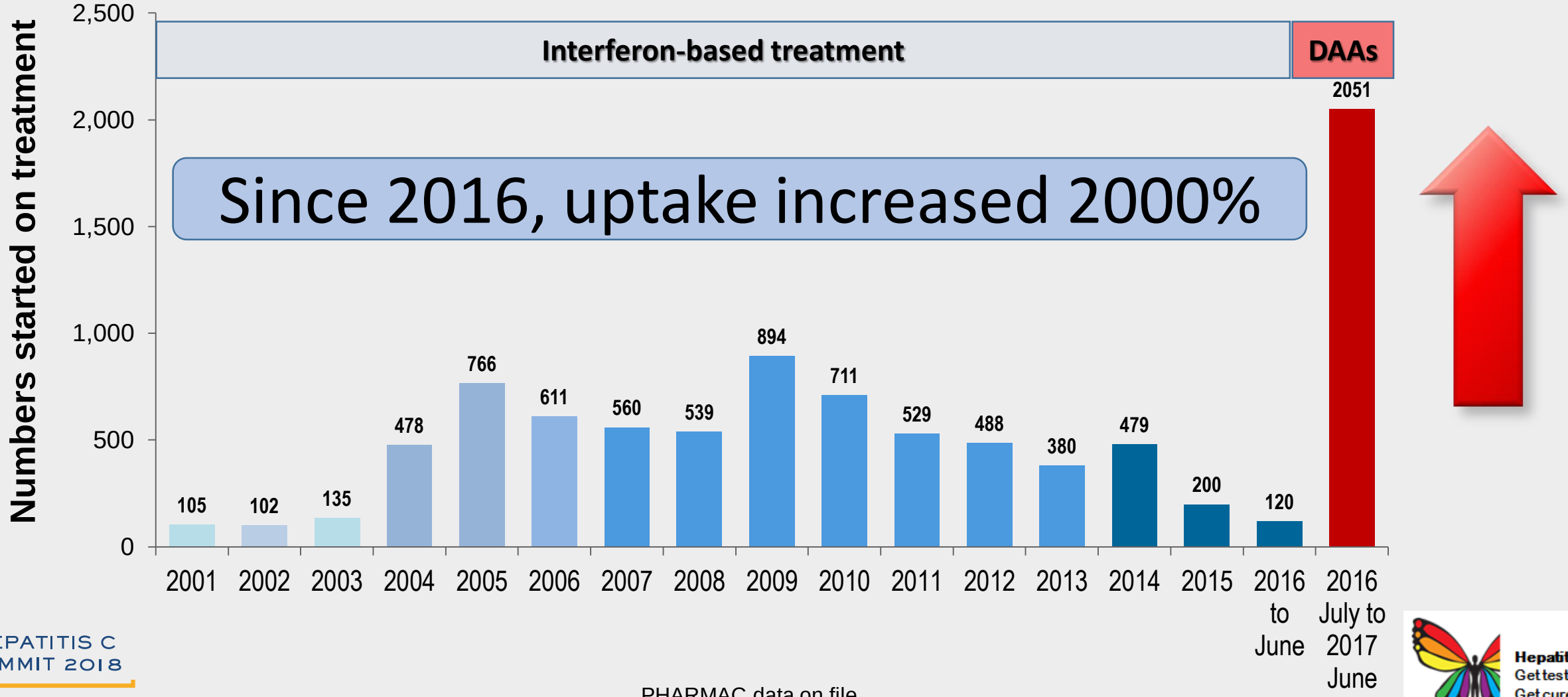
What do the 12 Countries on Track to Achieve Hepatitis C Elimination All Have in Common?

1. Access to effective treatment without restriction
2. Treating 7-10% infected population annually
3. Harm reduction programs to reduce new infections
4. National HCV screening programs
5. National registries linking diagnosis to treatment
6. Expanding treatment to community prescribers

CDA 2018: Polaris Observatory (http://centerforda.com/polaris/)

Can NZ Reach the WHO 2030 Elimination Targets?

Treatment Uptake has Increased Following Funding of VIEKIRA PAK in July 2016



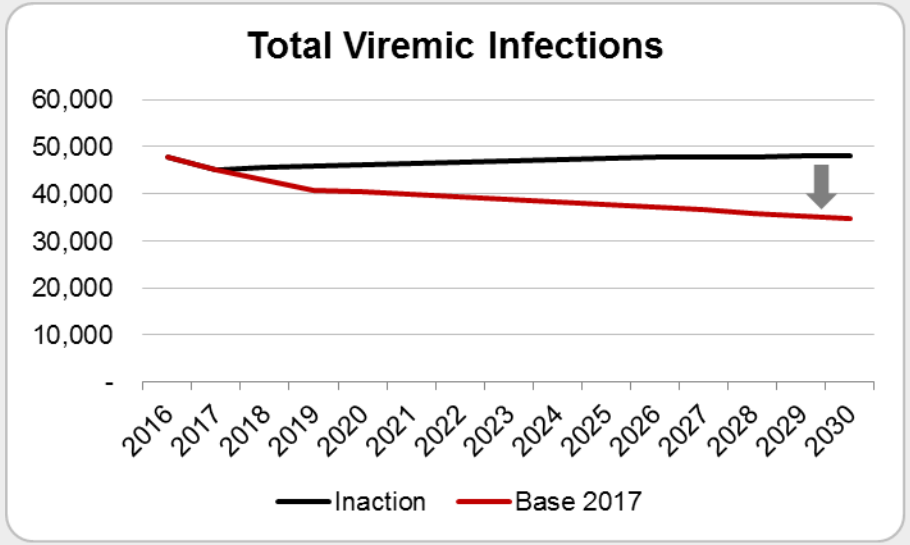
PHARMAC data on file

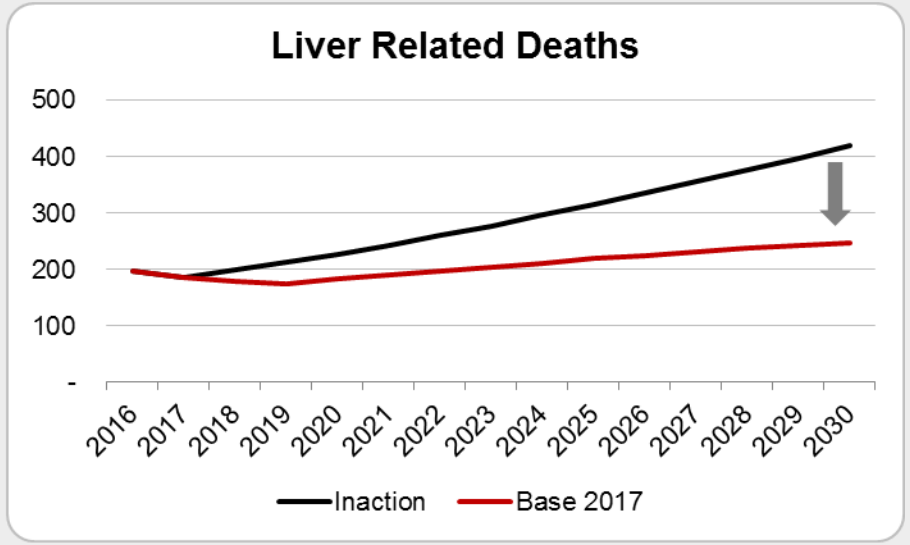
Base 2017 (VIEKIRA PAK - G1 & HARVONI - decompensated G2-6)

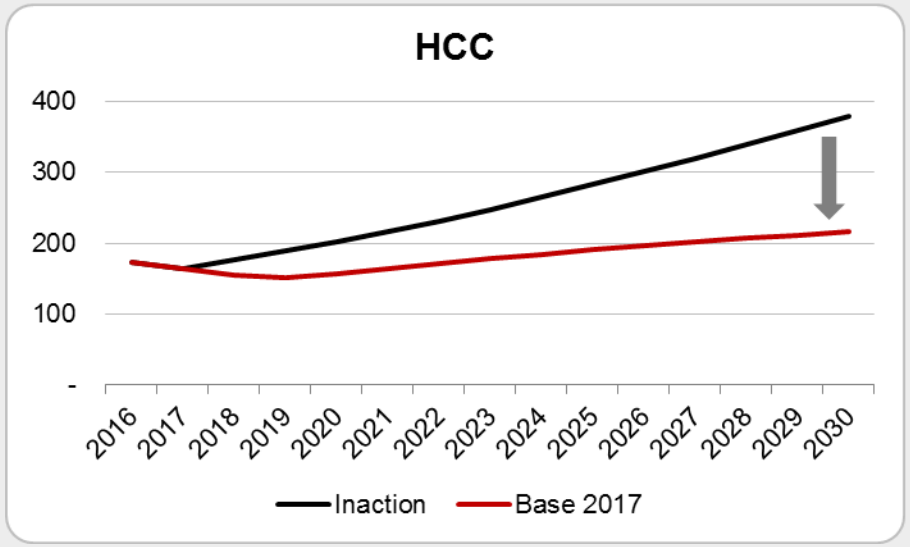
- Expanded treatment numbers increase to 3,000 patients in 2017 then declines as the diagnosed G1 population is depleted
- Newly diagnosed remains at current rate - 910 patients annually

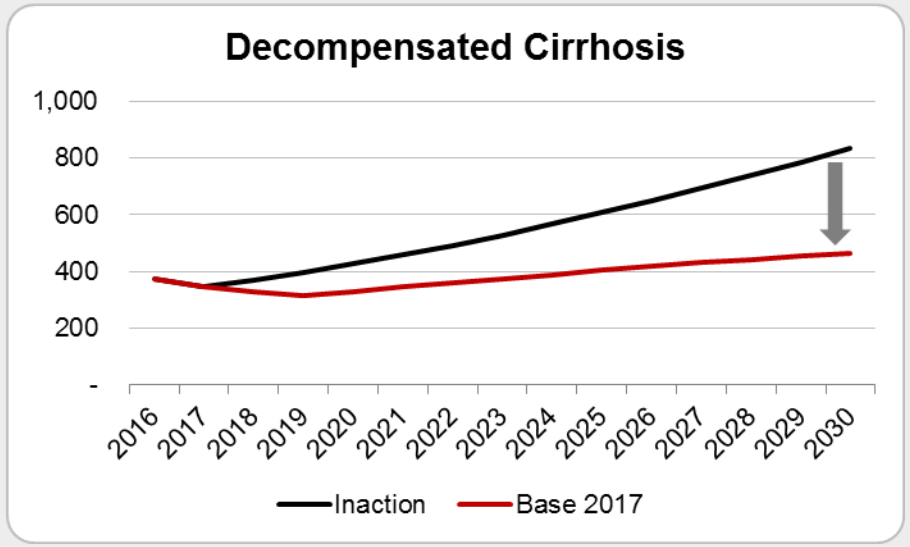
	2016	2017	2018	2019	≥ 2020
Treated	1,900	3,000	2,800	2,500	940
Newly Diagnosed	910	910	910	910	910
Fibrosis Stage G1 G2- G6	 ≥F0 ≥ Decomp	 ≥F0 ≥ Decomp	 ≥F0 ≥ Decomp	 ≥F0 ≥ Decomp	 ≥F0 ≥ Decomp
New Infections	1,000	1,000	1,000	1,000	1,000
Treated Age	15-74	15-74	15-74	15-74	15-74
SVR	97%	97%	97%	97%	97%

Base 2017 (VIEKIRA PAK - G1 & HARVONI - decompensated G2-6)









2017 Base – total infections will decrease by 23%. 1,200 deaths, 530 decompensated cirrhosis cases, & 680 HCC cases will be averted

Gane E, et al. *NZ Med J* 2014;127(1407):61–74.

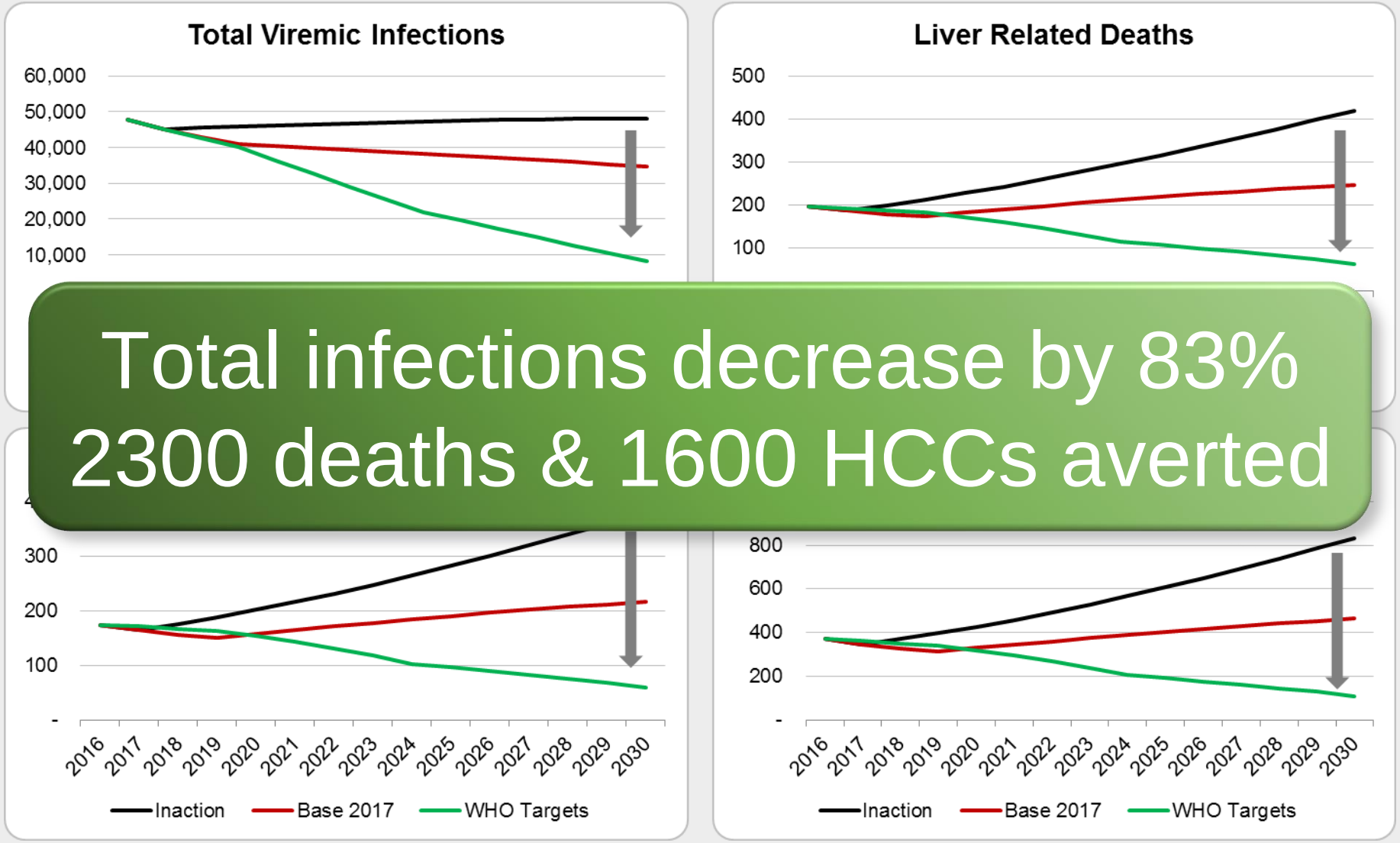
WHO Targets (requires funded pan-genotypic DAAS)

- Scenario which achieves WHO Targets of 65% reduction in liver related mortality and 90% diagnosis rate in infected population by 2030
- Increased treatment to 4,000 patients and diagnosis to 2,000 patients

	2016	2017	2018	2020	≥ 2025
Treated	1,900	3,000	3,000	4,000	2,200
Newly Diagnosed	910	910	2,000	2,000	2,000
Fibrosis Stage					
G1	≥F0	≥F0	≥F0	≥F0	≥F0
G2-G6	≥ Decomp	≥ Decomp	≥F0	≥F0	≥F0
New Infections	1,000	1,000	1,000	720	90
Treated Age	15-74	15-74	15-74	15-74	15-74
SVR	97%	97%	97%	97%	97%

Dr Homie Razavi unpublished model

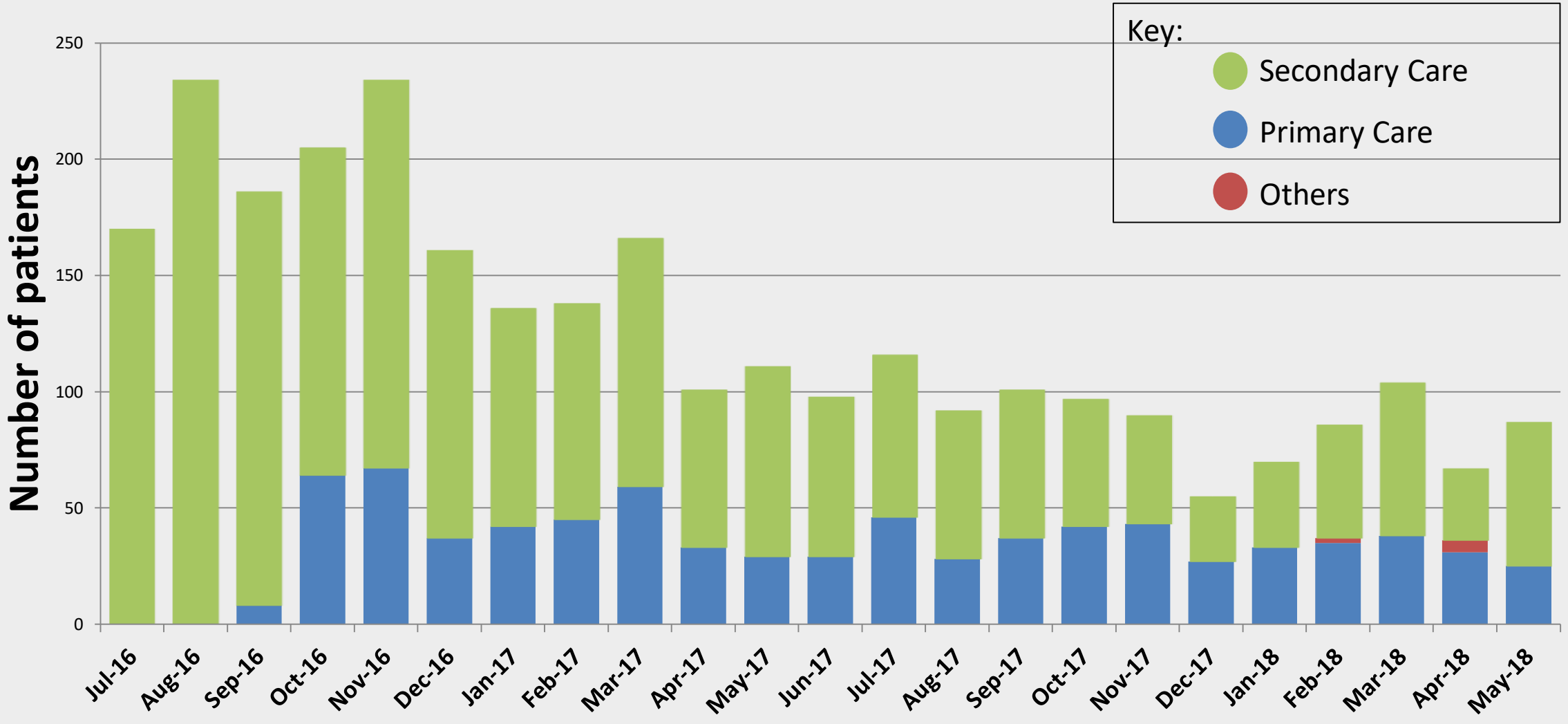
WHO Targets (requires funded pan-genotypic DAAS)



Total infections decrease by 83%
2300 deaths & 1600 HCCs averted

Gane E, et al. *NZ Med J* 2014;127(1407):61–74.

We Need to Increase Treatment Uptake



PHARMAC Data on file

How can we increase treatment uptake?

1. **Find the Undiagnosed**
2. Improve Linkage to Care
3. Access to Pangenotypic DAAs

2. Find the undiagnosed

1. **Targeted testing (ANZ/UK approach)**
   - Using recognised risk factors – IDU, tattoos, prison
   - Limited by stigma of IDU

2. **Birth Cohort Testing (US approach)**
   - Born 1945-65 “Woodstock” and Vietnam War era
   - Not relevant in most countries

3. **Universal Testing (French approach)**
   - Cost-effective only if we have a national registry and access to cheaper diagnostics

How can we increase treatment uptake?

1. Find the Undiagnosed
2. **Improve Linkage to Care**
3. Access to Pangenotypic DAAs

3. Improve Linkage to Care

- Move treatment from hospital into community

1. Safer
   - GPs and nurses know medical and psychosocial comorbidities
   - GPs and nurses know co-meds ⇨avoid drug-drug interactions
2. Reduced travel and costs
   - Less travel
   - GP payment from DHB POACS
   - Patient payment from WINZ
3. Increased awareness and testing
4. Reduced stigmatisation

How can we increase treatment uptake?

1. Find the Undiagnosed
2. Improve Linkage to Care
3. **Access to Pangenotypic DAAs**

Introduction to MAVIRET

Glecaprevir (GLE)

pangenotypic NS3/4A protease inhibitor

Pibrentasvir (PIB)

Pangenotypic NS5A inhibitor

Glecaprevir/pibrentasvir approval was based on clinical trial data in over 2,300 patients including placebo and active-controlled studies

Glecaprevir/pibrentasvir is a fixed-dose combination of glecaprevir, an HCV NS3/4A protease inhibitor, and pibrentasvir, an HCV NS5A inhibitor, and is indicated for the treatment of patients with chronic HCV GT 1, 2, 3, 4, 5 or 6 infection without cirrhosis and with compensated cirrhosis (Child-Pugh A)

Maviret is indicated for the treatment of adult patients with chronic HCV GT 1, 2, 3, 4, 5 or 6 infection without cirrhosis and with compensated cirrhosis (Child-Pugh A)

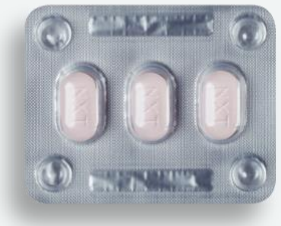
GT=genotype. HCV=hepatitis C virus. NS=non-structural protein.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz

MAVIRET glecaprevir/pibrentasvir

Formulation & Packaging

- Co-formulated, film-coated tablet of glecaprevir (100mg) and pibrentasvir (40mg)
- **Recommended oral dose is 3 tablets taken once daily with food**
- Tablets should be taken whole and not chewed, crushed or broken



Daily blister sheet

Weekly carton

Monthly carton (28 Days)

MAVIRET Data Sheet. Available at www.medsafe.govt.nz

MAVIRET glecaprevir/pibrentasvir

Registrational Trials of Maviret in >2,300 Adults with HCV Gt 1–6

		Population	N	Treatment	Prior treatment*	Cirrhosis status
PHASE 2	MAGELLAN-I	GT 1, 4	113	MAVIRET for 12 or 16 weeks	DAA-exp	NC, CC
	SURVEYOR-I	GT 1, 4, 5, 6	66	MAVIRET for 8 or 12 weeks	TN, TE	NC
	SURVEYOR-II	GT 2, 3, 4, 5, 6	590	MAVIRET for 8, 12, or 16 weeks	TN, TE	NC, CC
PHASE 3	ENDURANCE-1	GT 1	703	MAVIRET for 8 or 12 weeks	TN, TE	NC
	ENDURANCE-2	GT 2	302	MAVIRET for 12 weeks vs PBO	TN, TE	NC
	ENDURANCE-3	GT 3	505	MAVIRET for 8 or 12 weeks; DCV+SOF for 12 weeks	TN	NC
	ENDURANCE-4	GT 4, 5, 6	121	MAVIRET for 12 weeks	TN, TE	NC
SPECIAL POPULATIONS	EXPEDITION-1	GT 1, 2, 4, 5, 6	146	MAVIRET for 12 weeks	TN, TE	CC
	EXPEDITION-4	GT 1, 2, 3, 4, 5, 6; CKD	104	MAVIRET for 12 weeks	TN, TE	NC, CC

Sustained virologic response (SVR12), defined as HCV RNA below the lower limit of detection at 12 weeks post end-of-treatment, was a primary efficacy endpoint of all studies.

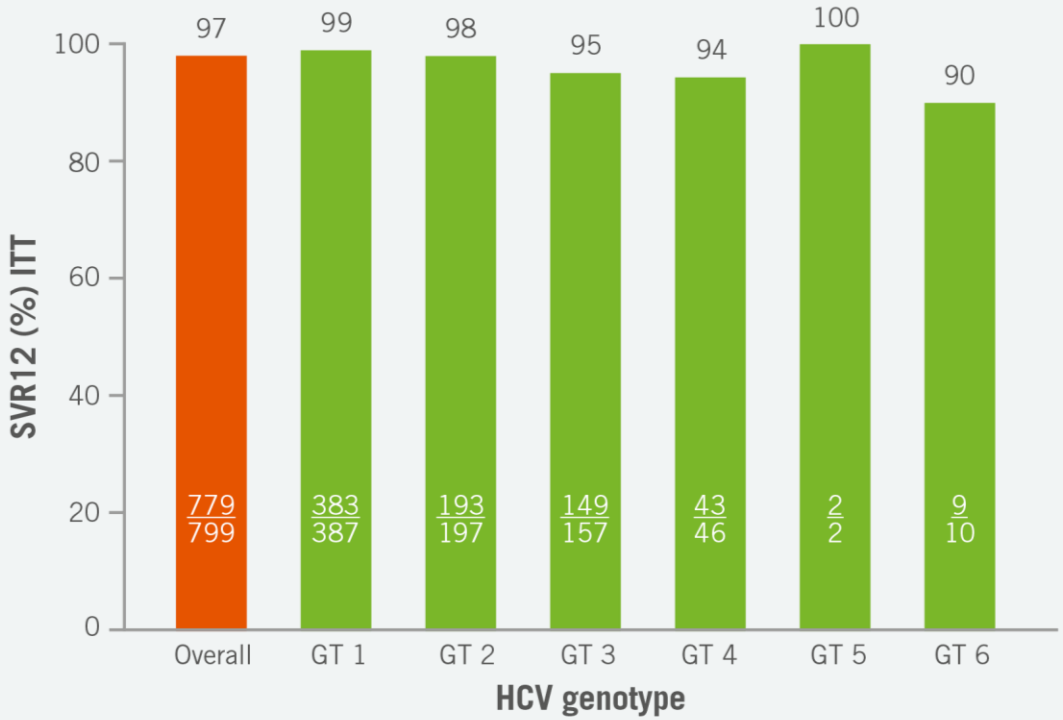
CC=compensated cirrhosis. CKD=chronic kidney disease. DAA=direct-acting antiviral. DCV=daclatasvir. GT=genotype. HCV=hepatitis C virus. NC=noncirrhotic. PBO=placebo. RNA=ribonucleic acid. SOF=sofosbuvir. SVR=sustained virologic response. TE=treatment-experienced. TN=treatment-naive.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz

MAVIRET glecaprevir/pibrentasvir

Integrated Analysis of Non-cirrhotic Patients with HCV GT 1–6

MAVIRET once daily for 8 Weeks (ITT)



BT	2	1		1			
Relapse	7		2	5			
Non-VF†	11	3	2	2	3		1

High SVR12 rates were achieved with 8 weeks of MAVIRET in treatment naïve* non cirrhotic patients irrespective of HCV genotype

GT 1, 2, 4, 5 and 6 patients includes patients experienced with prior regimens containing peginterferon, ribavirin, and/or sofosbuvir.

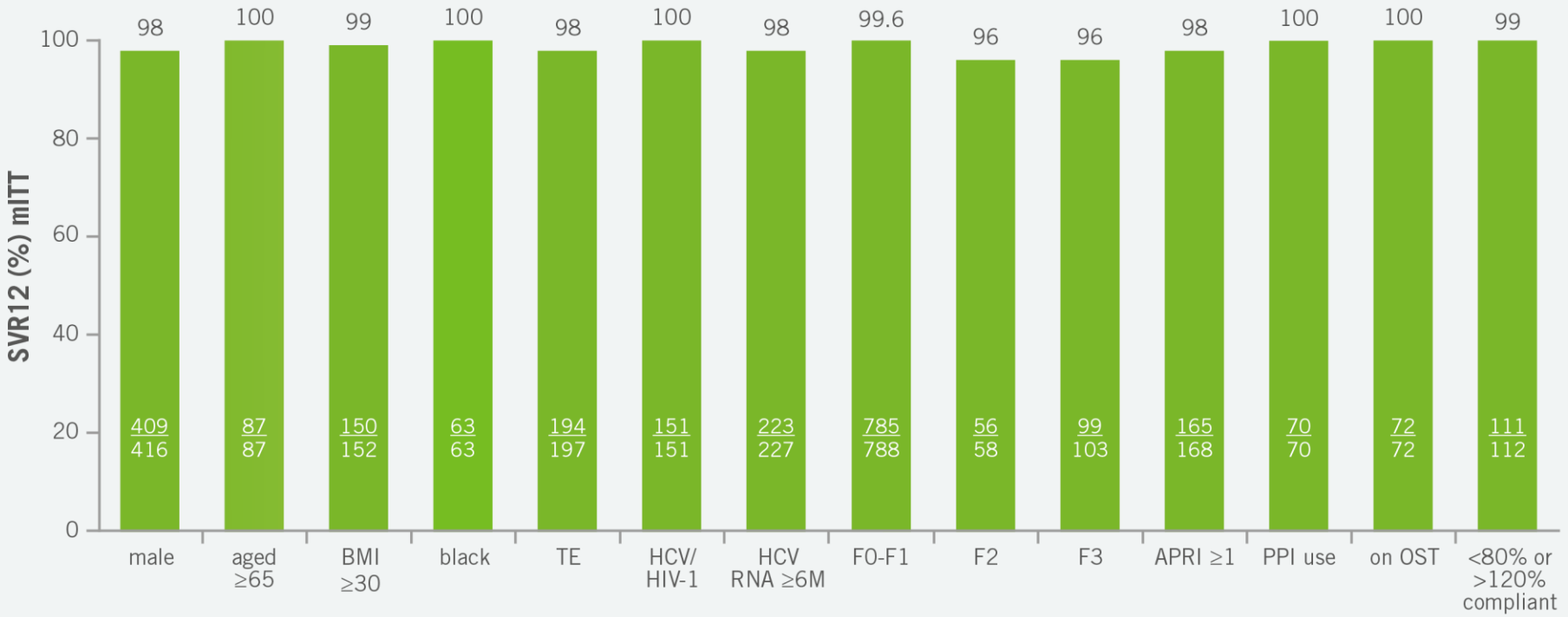
BT=breakthrough. GT=genotype. ITT=intent-to-treat.. SVR=sustained virologic response. TN=treatment-naïve. VF=virologic failure.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz
Puoti M et al. J Hepatol 2018; doi: 10.1016/j.hep.2018.03.007

MAVIRET glecaprevir/pibrentasvir

Integrated Analysis of Non-cirrhotic Patients with HCV GT 1–6

MAVIRET once daily for 8 Weeks (ITT)



High SVR12 was achieved irrespective of baseline patient and viral characteristics

APRI=aspartate aminotransferase to platelet ratio. BMI=body mass index. GT=genotype. HCV=hepatitis C virus. HIV=human immunodeficiency virus. mITT=modified ITT (excludes patients with non virologic failure). OST=opioid substitution therapy. pegIFN=peginterferon. PPI=proton pump inhibitor. RBV=ribavirin. RNA=ribonucleic acid. SVR=sustained virologic response. SVR12=HCV RNA below the lower limit of detection at 12 weeks post end-of-treatment. TE=treatment experienced.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz
Puoti M et al. J Hepatol 2018; doi: 10.1016/j.hep.2018.03.007

MAVIRET glecaprevir/pibrentasvir

Treatment Duration depends on cirrhosis and previous IFN

Patient populations	Recommended Treatment Duration
GT 1,2,3,4,5 or 6 without cirrhosis	8 weeks
GT 1,2,3,4,5 or 6 with cirrhosis	12 weeks
IFN-Failure GT 3 with or without cirrhosis	16 weeks

GT=genotype. HCV=hepatitis C virus. HIV=human immunodeficiency virus

MAVIRET Data Sheet. Available at www.medsafe.govt.nz

MAVIRET glecaprevir/pibrentasvir

Maviret – length of treatment

- Well compensated cirrhosis - 12 weeks treatment (treat through hospital)
- Genotype 3 or Treatment experienced - 16 weeks treatment (treat through hospital)

EVERYONE ELSE

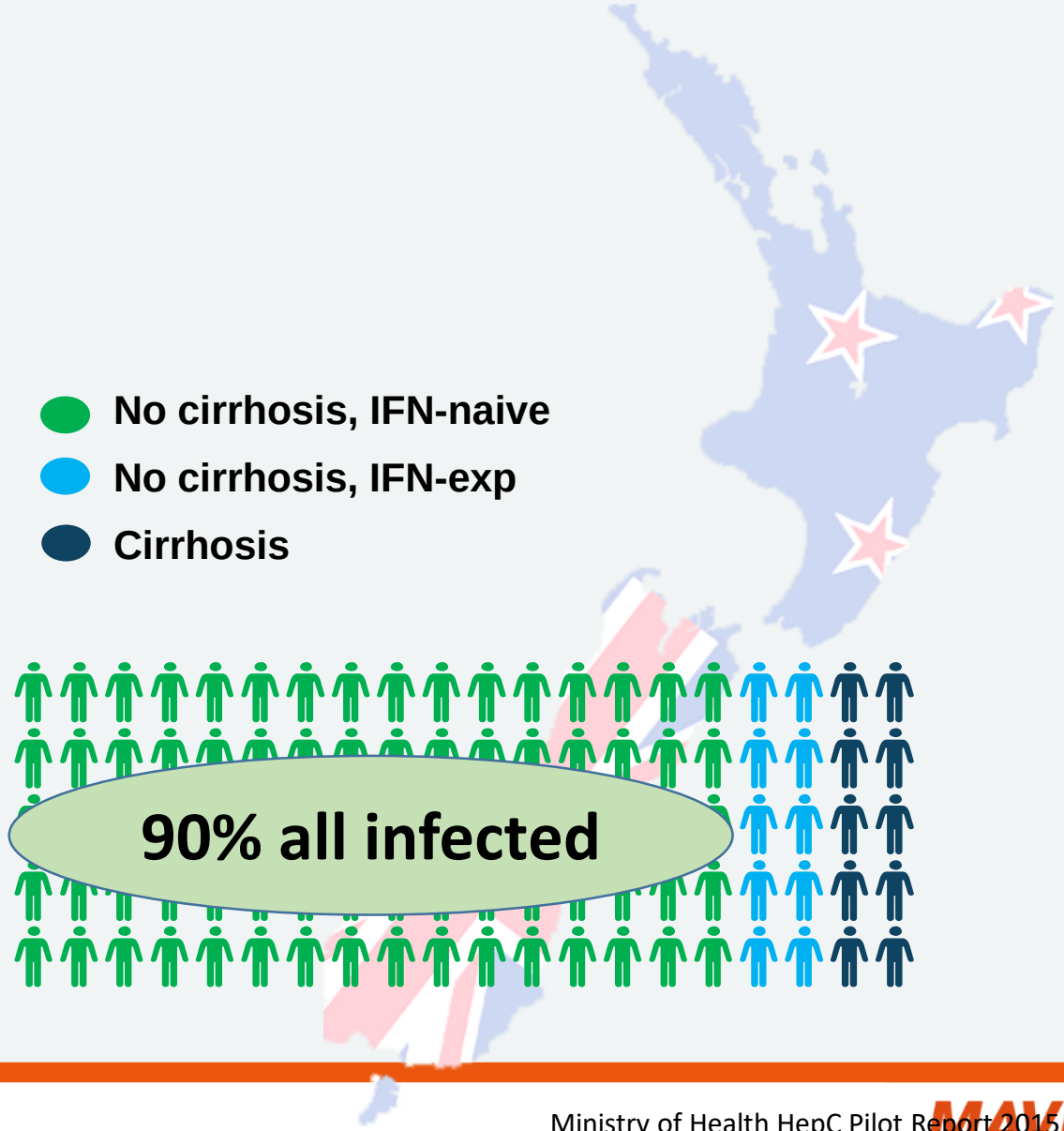
- 8 weeks treatment

>98.5% CURE

Who is suitable for 8 weeks treatment in 2019

50,000

New Zealanders live with chronic HCV infection



Ministry of Health HepC Pilot Report 2015

abbvie

MAVIRET glecaprevir/pibrentasvir

VIEKIRA PAK Drug-drug interactions

Contraindicated
Alfuzosin hydrochloride
Aliskerin
Atorvistatin
Bosentan
Budesonide
Carbamazepine
Cisapride
Domperidone
Dronedarone
Efavirenz
Ergotamine
Ethinyloestradiol
Fusidic Acid
Gemfibrozil
Fluticasone
Etravirine
Gemfibrozil
Indinavir
Lopinavir

Contraindicated
Lovastatin
Midazolam (oral)
Nevirapine
Phenytoin
Pimozide
Ranolazine
Rifampicin
Rilpivirine
Ritonavir
Salmeterol
Sildenafil*
Simvastatin
Salmeterol
St. John's Wort
Tacrolimus
Terfenadine
Triazolam
Phenytoin

Contraindicated
Lovastatin
Midazolam (oral)
Nevirapine

Caution/adjust/ monitor
Alprazolam
Ambristentan

Caution/adjust/ monitor
Ezetamide
Fludrocortisone
Fluvastatin
Furosemide
Nelfinavir

Caution/adjust/ monitor
Norethisterone
Phencyclidine
Omeprazole§
Pravastatin

MAVIRET DDIs

Contraindicated
Atazanavir
Rifampicin

Caution/adjust/ monitor
Atorvistatin
Cyclosporin
Dexamethasone
Efavirenz
Ethinyloestrodiol
Ezetimide
Indinavir
Lopinavir
Nevirapine
St Johns Wort

***This is not an exhaustive list please refer to the full MAVIRET data sheet www.medafe.govt.nz & The University of Liverpool Hep Drug Interactions www.hep-druginteractions.org. In some instances, the recommendations in the data sheet may differ to those on the University of Liverpool Hep Drug Interactions website.**

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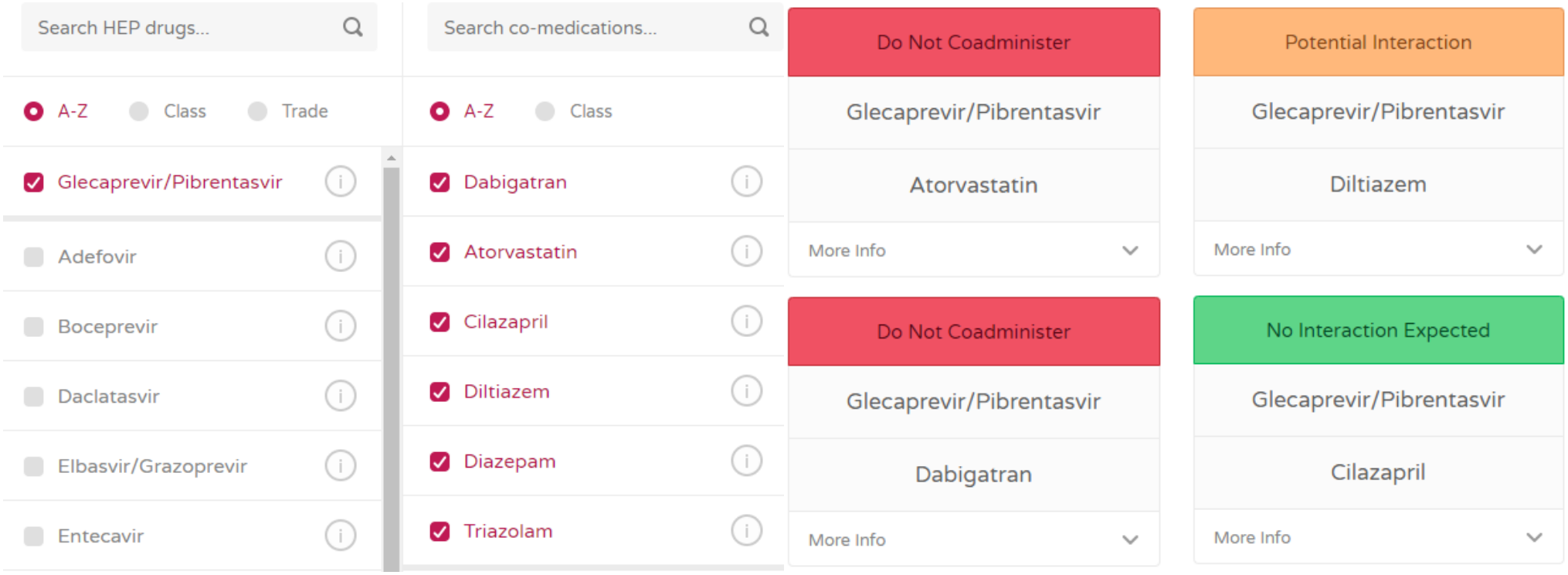
MAVIRET glecaprevir/pibrentasvir

www.hep-druginteractions.org



MAVIRET should improve treatment uptake

- **Simplified regimens for noncirrhotic patients**
  - 8 weeks MAVIRET
  - Once daily dosing, no ribavirin
- **Simplified pre-treatment assessment**
  - No HCV quantitation, genotype or RAS testing
  - Could use HCV antigen test (at LabTests)
- **Simplified on-treatment management**
  - Minimal Drug-drug interactions
  - No on-treatment monitoring
- **Simplified post-treatment management**
  - Need for SVR12 when <1% failure?

Previous Treatment

Assessing Liver Health

APRI or Transient Elastography

AST to Platelet Ratio Index (APRI) Calculator

Share

This is an **A**ST to **P**latelet **R**atio **I**ndex (APRI) calculator tool. Enter the required values to calculate the APRI value. The APRI Score will appear in the oval on the far right (highlighted in yellow). Most experts recommend using 40 IU/L as the value for the AST upper limit of normal when calculating an APRI value.

$$\text{APRI} = \frac{\dfrac{\text{AST Level } (IU/L)}{\text{AST (Upper Limit of Normal) } (IU/L)}}{\text{Platelet Count } (10^9/L)} \times 100 =$$

APRI <0.85 consistent with no cirrhosis

APRI >1.0 likely cirrhosis

(NZ Society Of Gastroenterology HCV Treatment Guidelines)

Liver Elastography – Fibroscan or ShearWave Elastography

- Fibroscan (mobile) and SWE (MMH only)
  - Noninvasive test
  - No prep involved
  - Takes 5 – 10 minutes
  - Immediate results
- Request by e-referral
  - Graded <6 weeks, but currently no waiting list
- Drop in clinics at CADS, ACSF and ARWCF

Jacqui Stone
Nurse Practitioner

Lucy Mills
Clinical Nurse Specialist

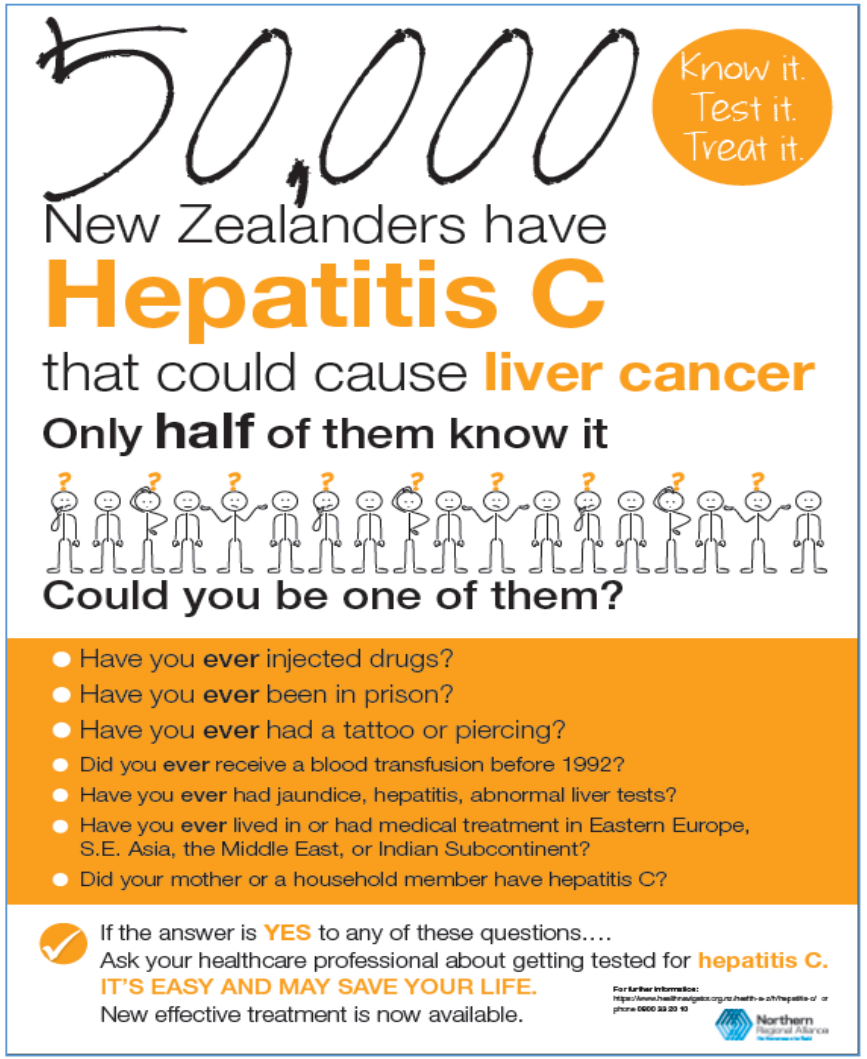
The Future…Our vision

- Be part of WHO target for Hep C eradication as a Public threat by 2030
- Community based testing and treatment
- Rapid Testing – results within an hour
- Prescription straight away for treatment if positive
- Easy accessible treatment for ALL!

Where to next?

- Finding the 50% who unknowingly have Hepatitis C
  - Contact Tracing
  - Alcohol Abuse
  - Tattoos or piercings
  - Recreational Drug use
  - Medical Tourists
  - Unexplained lethargy

Who Should Get Tested?



Summary

- Maviret is simple to use and is well tolerated
- Most people only need 8 weeks treatment and results are excellent
- Very few drug to drug interactions
- No blood monitoring required unless cirrhotic (and they should be treated at hospital anyway)
- ***Need to find the undiagnosed***

Acknowlegements

- Lucy Mills CNS Counties Manukau
- Dr Ed Gane NZLTU Auckland City Hospital
- AbbVie

“All right, let's not panic.
I'll make the money by selling one of my livers.
I can get by with one “

Doh!