# The Epidemiology of IDU associated IE

- Typical case
- Historical perspective
- Lessons from ICE
- Recent trends
- Policy
- War on drugs
- Harm reduction
- Decriminalisation
- Future

Professor Eugene Athan
Barwon Health Endocarditis Service and Deakin University
Australia

## No relevant disclosures

# Case Ms TS 44 year old grandmother

- IDU > 10 years heroin, crystal methamphetamine
- 2005 AVIE S. aureus epidural abscess laminectomy
- 2006 S oralis IE
- 2007 AVR bioprosthetic non urgent for worsening AR
- 2013 Redo AVR
- 2018 PVIE aortic root abscess Corynbacteria sp sens to Penicillin
  - Cerebral infarcts
  - Lifelong amoxil
  - Alive 10/2018

# Historical perspective

- Am J Med 1950 Hussey and Katz Gallinger Hospital Washington DC
- Described medical complications in heroin addicts from 1938-1947
- 28% of all cases
- Previously most treated psychiatry
- Cutaneous abscess, thrombophlebitis, septicaemia, endocarditis in 8 cases, tetanus (fatal first in 1924 JAMA) malaria
- Mostly African American
- Preparation mixed with water, not boiled, cocaine other
- Communal sharing injecting equipment the norm
- S aureus, right sided, pulmonary infarction XR treated penicillin no murmurs
- 4 of 8 died autopsy

#### **IDU** associated IE

- IDU remains an important risk factor for IE
- Diagnostic criteria Modified Duke criteria.
- Colonisation with S. aureus commonest organism implicated in IDU IE and risk factor for infection
- Common among IDU vs general population Tuazon, Gordon NEJM 2005
- Increased rate of carriage of S. aureus among Narcotic Addicts Tuazon and Sheagren. JID 1974.
- 35% of those who had injections within 1 week of culture.

## Lessons from ICE



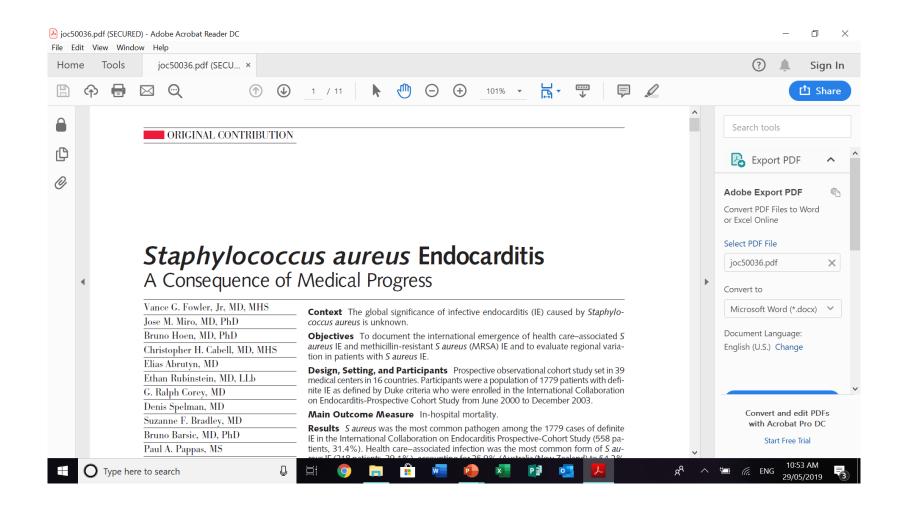
International Collaboration on Endocarditis

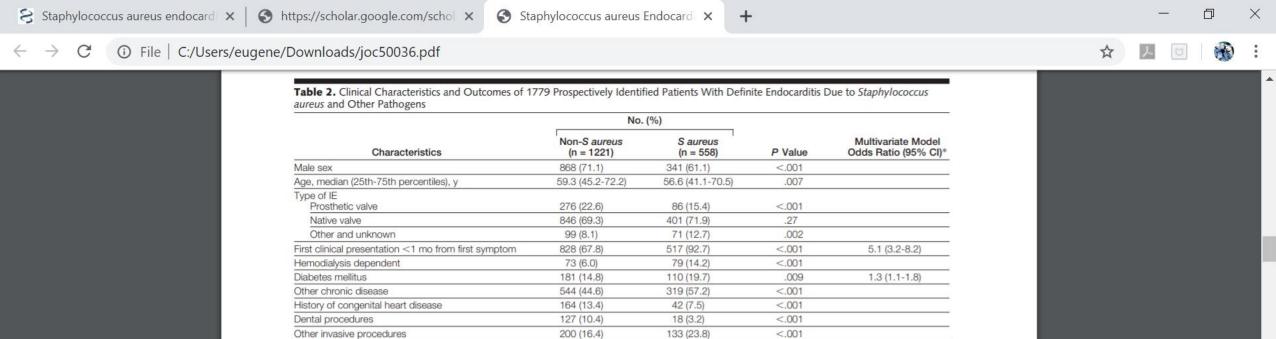
Clinical Presentation, Etiology and Outcome of Infective Endocarditis in the 21st Century: The International Collaboration on Endocarditis-Prospective Cohort Study. Murdoch et al for ICE. Arch Intern Med. 2009.

#### Current IV drug use

- 268/2746 (10) overall
- 93/587 (16) North America
- 1/249 (0.4) South America
- 113/1203 (9) Europe
- 61/707 (9) Asia/Pacific
- P < 0.001
- Lower In hospital mortality OR 0.93

Staphylococcus aureus Endocarditis. A Consequence of Medical Progress. Vance G. Fowler et al. JAMA 2005.



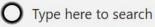


133 (23.8) Presumed intravascular device source† 112 (9.1) 159 (28.4) <.001 1.7 (1.2-2.6) Physical examination findings 259 (25.5) 162 (32.7) .003 Vascular/immunologic evidence of endocarditis‡ 224 (40.1) New or worsening of old cardiac murmur 649 (53.2) <.001 113 (20.3) Septic pulmonary infarcts 50 (4.1) <.001 Echocardiographic findings Intracardiac vegetations 1027 (84.1) 492 (88.2) .05 504 (49.1) 143 (29.1) <.001 Aortic Mitral 490 (47.7) 224 (45.5) .37 Tricuspid 77 (7.5) 128 (26.0) <.001 Pulmonic 4 (0.8) .63 11 (1.1) 87 (8.5) .005 Other 62 (12.6) Paravalvular complications 310 (25.4) 113 (20.3) .02 Prosthetic paravalvular complications 113 (9.3) 29 (5.2) .004 New regurgitation 809 (66.3) 298 (53.4) <.001 Presumed place of acquisition Health care-associated§ 211 (17.3) 218 (39.1) <.001 2.9 (2.1-3.8) 938 (76.8) Community-acquired 326 (58.4) <.001 DU-associated 50 (4.1) 9.3 (6.3-13.7) 117 (21.0) <.001 Non-IDU-associated 888 (72.7) 209 (37.5) <.001

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Unknown









72 (5.9)





14 (2.5)





.002

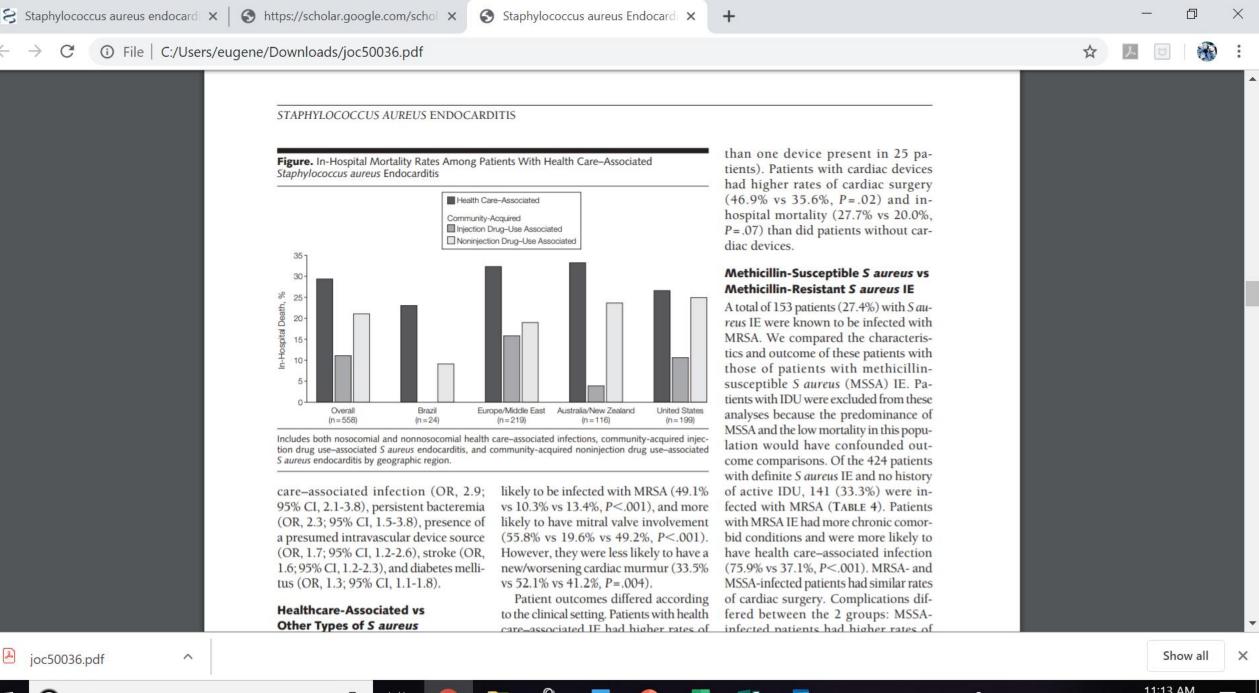




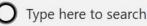








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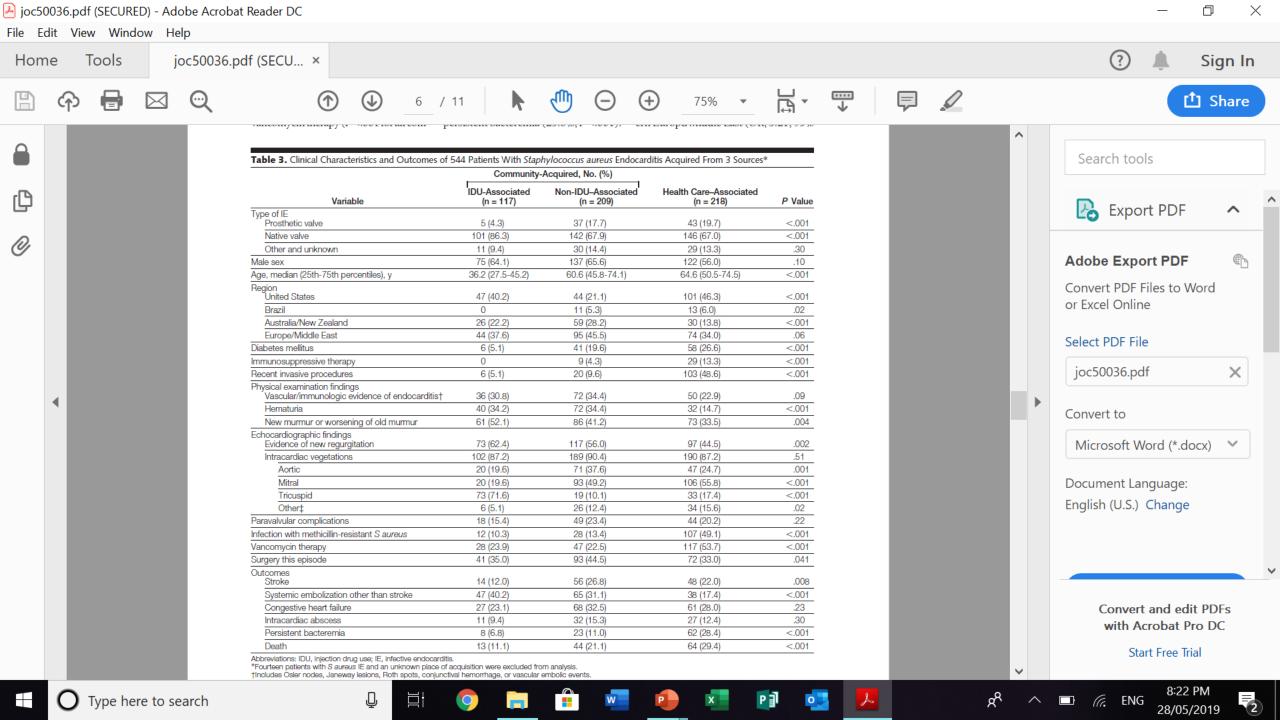












Repeat endocarditis: analysis of risk factors based on the International Collaboration on Endocarditis – Prospective Cohort Study. L. Alagna et al. CMI. 2013.

- Repeat episodes of IE can occur in patients who survive an initial episode.
- Analysed risk factors and 1-year mortality of patients with repeat IE.
- 1874 patients enrolled in ICE-PCS
- Cohort Study between January 2000 and December 2006 (ICE-PCS) with definite native or prosthetic valve IE and 1-year follow-up

# Bivariate analysis patients with repeat IE were more likely:

- Younger
- North America
- Haemodialysis
- HIV infected
- History of IDU (p < 0.001)
- Previous endocarditis before enrollment into ICE PCS
- S. aureus IE (p 0.003) and tricuspid valve involvement (p < 0.001).
- Associated with non-nosocomial healthcare acquisition
- Cardiac surgery performed after discharge during the 1-year follow-up

# Multivariable model patient characteristics independently associated with repeat IE

- Haemodialysis (OR, 2.5; 95% CI, 1.2–5.3)
- IDU (OR, 2.9; 95% CI, 1.6–5.4)
- History of previous IE (OR, 2.8%; CI, 1.5–5.1)
- North America vs. Europe; OR, 1.9; 95% CI, 1.1–3.4).
- One-year survival for patients with repeat IE was 80%

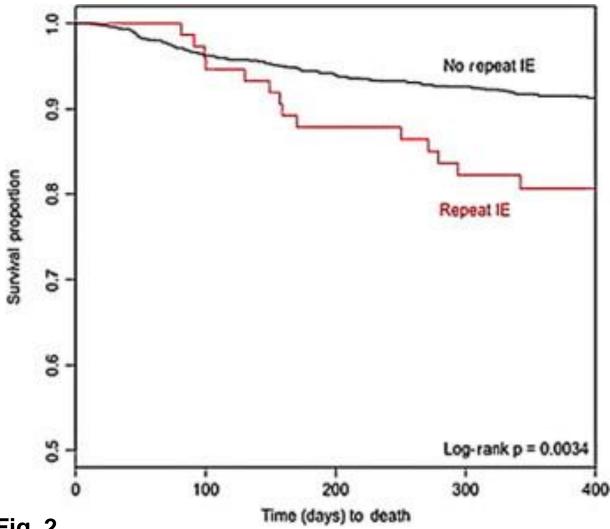


Fig. 2
Kaplan Meier survival curve for patients with repeat and single episode IE (no repeat IE).

### IE and HIV Wilson et al JID 2002

- Johns Hopkins urban cohort in Baltimore ALIVE (AIDS link to intravenous experiences) 3000 in late 1980s risk of IE according to HIV status
- Incidence of 13.8 vs 3.3 cases IE/1000 person years
- MV analysis: low CD count, women, increased injecting frequency

# Increased hospitalisations for IDU related IE Cooper et al CID 2007

- Increase over 66% between 2000 and 2003
- CDC National Hospital Discharge survey database
- Nationally representative annual data on hospitalisations
- Captures 270,000 inpatient stays
- ICD codes IE, drug dependence complex algorithm
- Injecting population remains stable
- Increased cocaine and methamphetamine use (vasospasm and myocardial injury) and HIV
- Decreased price heroin 1995 \$400 /g to \$240/g in 2002
- Increased CA-MRSA

Trends in Drug Use—Associated Infective Endocarditis and Heart Valve Surgery, 2007 to 2017: A Study of Statewide Discharge Data. A Schranz, Fleischauer, VH Chu, LT Wu, D L Rosen. Annals Int Med 2018.

- North Carolina hospitals 2007 to 2017 coding
- Rising rates of hospitalisations for IDU-IE (11% if IE admissions)
- Annual DUA-IE hospitalizations increased 0.92 to 10.95 100000 persons - 12 fold increase.
- Surgery for DUA-IE from 0.10 to 1.38 per 100 000 persons.
- Increased younger, female, white.
- Hospital stays for DUA-IE were longer (median, 27 vs. 17 days), with higher median charges (\$250 994 vs. \$198 764).
- Cost DUA-IE hospitalizations > \$78 million.

Evolving epidemiology of injecting drug use-associated infective endocarditis: A regional centre experience. Tung MK, Light M, Giri R, Lane S, Appelbe A, Harvey C, Athan E. Drug Alcohol Rev. 2015

- Retrospective analysis of two cohorts of consecutive patients (n = 226) admitted with IE from 2002 to 2013.
- Numbers of cases and rates of IE were compared (2002-2006 and 2009-2013).
- Rate ratios were calculated using Poisson distributions and to examine relationship over time.
- 130 cases of IE were seen in the first observation period (6 IDU-IE) and 96 in the second observation period (15 IDU-IE). The estimated incidence rate of IE had fallen from 10.1 to 6.45 per 100, 000 person-years [rate ratio 0.64, 95% confidence interval (CI) 0.48, 0.85].
- Incidence rate of IDU-E has risen from 0.48 to 0.79 per 100, 000 person-years (rate ratio 1.65, 95% CI 0.59, 4.57).
- Incidence rate regression suggests that the number of IDU-IE cases is expected to increase by a factor of 1.25 (95%CI 1.09-1.44) for each increase of 1 year.
- Over the last decade a rise in rate and number of cases of IDU-IE. This may indicate increasing IDU or increased rates of IE in IDUs in this region.

The Economic Burden of Infective Endocarditis due to Injection Drug Use in Australia. A Single Centre Study - University Hospital Geelong, Barwon Health. O Otome, A Wright, V Gunjaca, S Bowe, E Athan. Submitted.

- Our centre 2002-2014
- Poor health seeking behavior 23 episodes
- Presenting late > 70% (17/23) admitted to ICU
- 88% (15/17) were ventilated severe infection due to sepsis.
- 50% underwent valve replacement surgery
- Median ICU LOS was 4 days (IQR; 2 to 40)
- Median hospital LOS was 40 days (IQR; 5 to 119).
- >70% had hospital LOS > 4 weeks.
- Median cost of \$AUD 61,363 per admission
- The estimated state-wide cost in 2010 \$AUD16 million.

The Current Epidemiology of Injecting Drug Use-Associated Infective Endocarditis in Victoria, Australia in the Midst of Increasing Crystal Methamphetamine Use. Wright A, Otome O, Harvey C, Bowe S, Athan E. Heart Lung Circ. 2018.

#### Victoria over 6.4 million population

- Victorian Admitted Episode Dataset (VAED) was used to identify a population-based cohort with a diagnosis of IE and IDU-IE between 2009 and 2014 in Victoria. Incidence rates were calculated per 100,000 people/year.
- Rate ratios were calculated using Poisson distributions, and chi squared (χ2) test for trend were calculated to identify significant linear trends.
- Incidence rate of IE has risen significantly from 11.09 to 13.56 per 100,000 people/year from 2009 to 2014 (rate ratio 1.22, 95% confidence interval (CI) 1.10, 1.36, p < 0.001).
- Incidence of IDU-IE risen significantly from 0.92 to 1.76 per 100,000 people/year from 2009 to 2014 (rate ratio 1.93, 95% CI 1.28, 2.90, p = 0.002).
- The chi squared ( $\chi$ 2) test for trend of both IE and IDU-IE significant linear trend (p = 0.0015 and 0.005 respectively).
- Men are twice as likely to be affected by IE overall. The elderly were found to be the most affected by IE overall (ages 75 to 79 years) with IDU-IE affecting a much younger age group (ages 30 to 34 years).
- Validation of hospital coding for IDU-IE was shown to have sensitivity of 77.2% (95% CI 64.8, 86.2).
- 2009 to 2014 there has been a significant increase in incidence of both IE overall and IDU-IE in Victoria.

# Data Nationwide Inpatient sample 2000-2013 US Wurcel et al. Tufts OFID 2016

- 5-8 million discharges per annum, community hospitals
- ICD codes IE, drug dependence, HCV
- No. IDU IE 3578 to 8530
- Proportion of IE stable 7-8% then increased 12% 2013
- Increase in young 15-34 steep increase 28% to 42% p<0.001</li>
- Increase in whites (80%) and females (53%)

Why? Increased PWID or behavioural

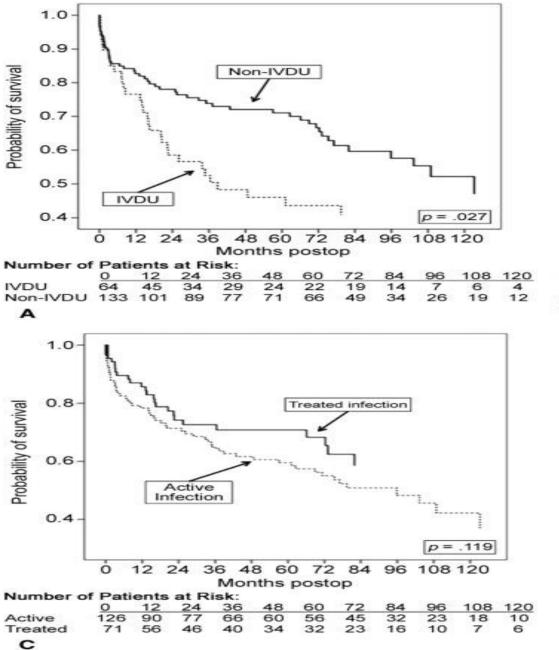
- Rates of opiate replacement therapy < 8%</li>
- ?Harm reduction strategies

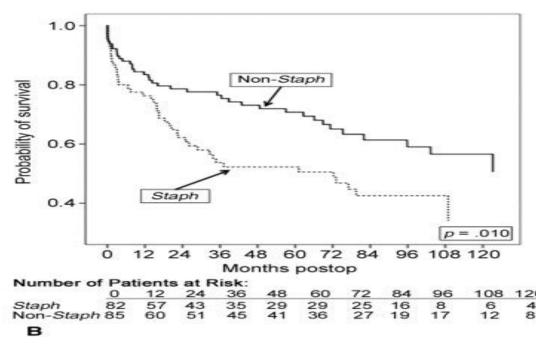
Long-term outcome for the surgical treatment of infective endocarditis with a focus on intravenous drug users. Rabkin et al. Annals Thoracic surgery 2012.

- 64 patients were identified as IVDUs and 133 patients as non-IVDUs.
- Survival at 30 days, 1 year, 5 years, and 10 years
- 91.2% vs 93.6%, 77.5% vs 83.0%, 46.7% vs 71.1%, and 41.1% vs 52.0%, respectively.
- Cox regression analysis identified IDU as an independent risk factor for diminished survival (p=0.03), although not for reoperation (p=0.95)
- 95.3% of IVDUs receiving bioprostheses versus 73.7% of non-IVDUs (p=0.0002, Fisher's exact test).
- 43 patients were identified as having preoperative septic cerebral emboli; none had a perioperative hemorrhagic event.
- Active infection approached significance as an independent risk factor for the composite end point of recurrent IE and perioperative infection.

#### CONCLUSIONS

- Bioprostheses are reasonable for IVDUs undergoing valve replacement for IE regardless of age.
- Prompt surgical intervention in the setting of septic cerebral emboli is justified; in the setting of active infection less clear.





# George H.W. Bush's biggest failure? The war on drugs.

How noble motives spawned destructive policies.



President George H.W. Bush holds a bag of crack cocaine in the Oval Office on Sept. 5, 1989, after delivering his first nationally televised speech. (Dennis Cook/AP)



#### By Matthew R. Pembleton

Matthew R. Pembleton is author of "Containing Addiction: The Federal Bureau of Narcotics and the Origins of America's Global Drug War" and teaches history at American University. December 6, 2018

There are good reasons to mourn the passing of George H.W. Bush. To many Americans, Bush was a decent man and a leader with integrity, a politician from a bygone era.

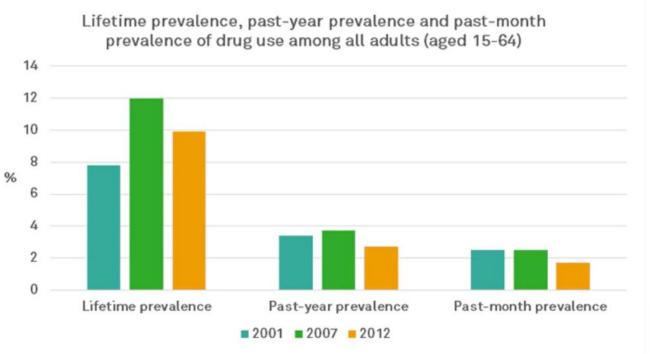
And Bush's complicated legacy does include much good, from his handling of the end of the Cold War to his support for climate science and the Americans With Disabilities Act. But it also includes some bad — specifically, a profound escalation in the War on Drugs. Ronald Reagan may have reoriented public attitudes about drugs when he pronounced in 1982, "Drugs are bad, and we're going after them . . . And we're going to win the war on drugs." But, it was Bush — and later, Bill Clinton — who put real resources into the effort.

When Bush took office, the federal drug control budget was around \$5 billion. When he left office in 1993, it was over \$12 billion. This was the sharpest escalation in the history of the drug war and it locked the country into a strategy of punishment, deterrence and intolerance. Based on instinct rather than evidence, Bush's approach did little to alleviate the public health crisis of addiction or halt the flow of drugs to American shores. And we remain trapped within this largely punitive approach today. So while we remember Bush as a "gentle soul," we should also remember his role in fomenting a drug war that harmed millions of American citizens, particularly in communities of color.

\$12 billion per annum growing Enforcement No benefits

### Portugal 14 Years after Decriminalizing all Drugs

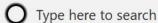
- 1980's government responded with a conservative approach vilified drug use and punitive set of policies led by the criminal justice system.
- 1999, nearly 1% of the population was addicted to heroin, and drug-related AIDS deaths in the country were the highest EU.
- 2001 decided to decriminalize possession and use of drugs
- In terms of usage rate and health, the data show that Portugal did not plunge into a drug crisis.
- Proportion of the population reports having used drugs at some point saw an initial increase after decriminalization, but then a steady decline.



Source: Transform Drug Policy Foundation

(Lifetime prevalence means the percentage of people who report having used a drug at some point in their life, past-year prevalence indicates having used within the last year, and past-month prevalence means those who've



















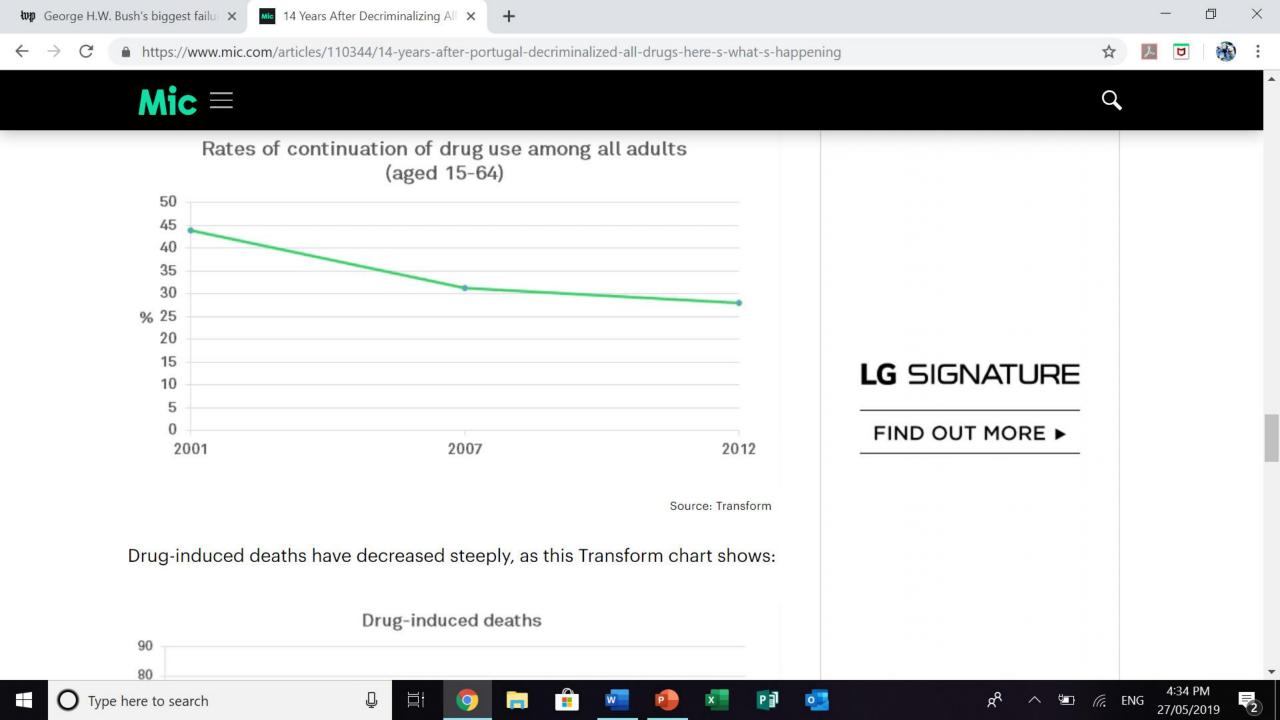


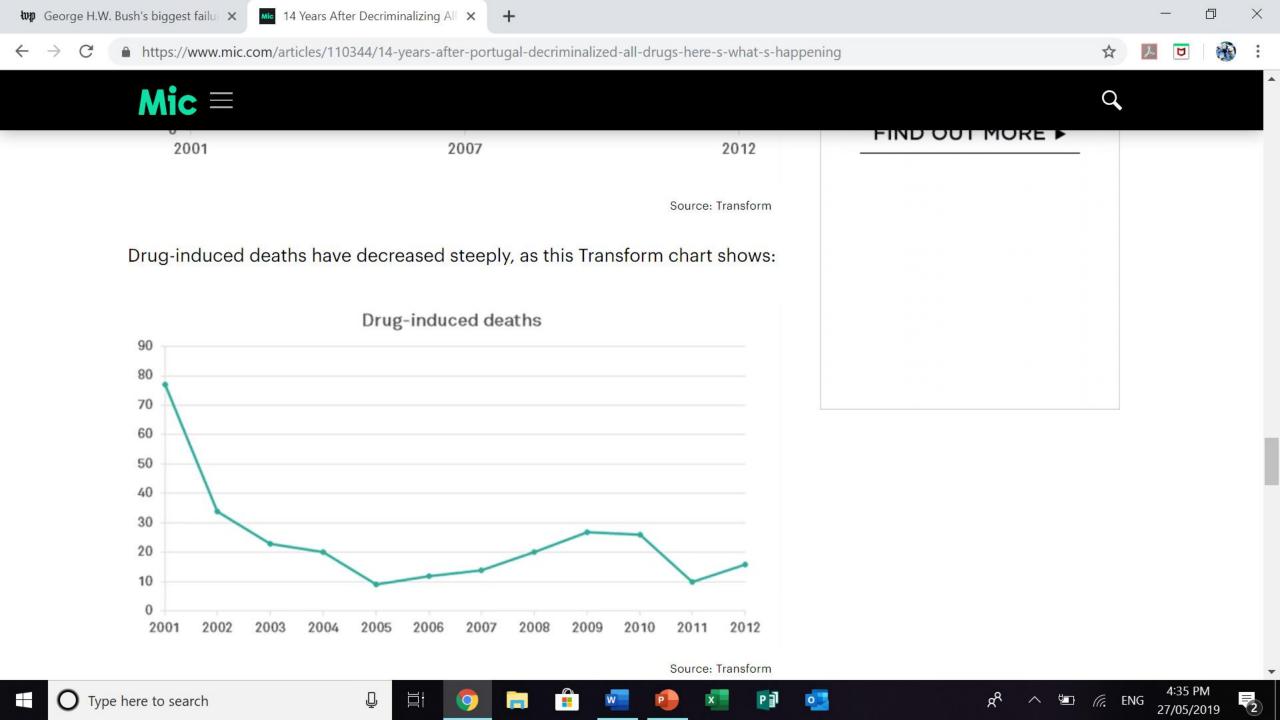


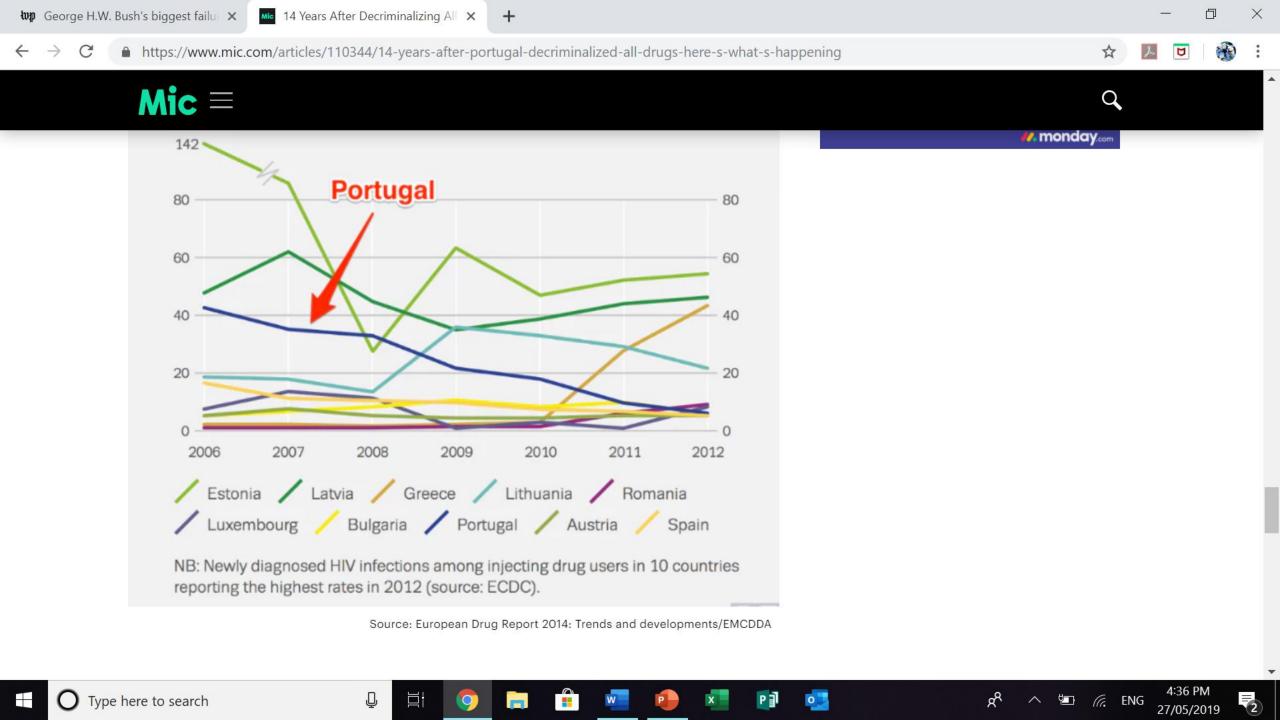












SINGAPORE (BLOOMBERG) - Malaysia's new strategy to combat drugs will focus on health and social support for users rather than enforcing criminal laws.

- Cabinet task force to address the drug problem met Jan 17 opinion that Malaysia's Dangerous Drugs Act 1952 needs to be reviewed and that drug use should be viewed as a social health issue, Minister Liew Vui Keong
- "Enforcement shouldn't hinge on trafficking of drugs and shouldn't rely on punishing those who are using the drugs," Liew said. Criminal enforcement has been ineffective, expensive and endangered the health of addicts.
- Change of approach Prime Minister Mahathir Mohamad's efforts to eradicate drug use, change related laws and abolish the death penalty.
- "Health-based approaches to drugs are shown to be cost-effective" and have a positive impact, Naomi Burke-Shyne, executive director of Harm Reduction International responding to the Malaysian initiative.

Separation of Drug Markets and the Normalization of Drug Problems in the Netherlands: An Example for other Nations? Henk Jan Van Vliet First Published July 1, 1990 Research Article

- Late 1960s, the Dutch have developed drug policies to try and solve social problems and be costeffective.
- Strategy led to an uneasy relationship with the international drug control system and with countries advocating "War on Drugs" policies.

#### Two basic elements:

- **Decriminalization** of the use of and the retail trade in cannabis
- Aims at keeping youngsters away from drugs like heroin, cocaine.
- This "separation of markets" concept, developed in the early 1970s, has proven to be a successful.
- **Normalization of drug problems** aims at the integration of drug abusers in society, in order to minimize the harm inflicted by drug abuse on the abuser, his environment and society.
- This policy element plays a paramount role in AIDS prevention.
- Statistics suggest that these policies are relatively successful in the Netherlands

Russian Federation: Talha Burki, "Russia's drug policy fuels infectious disease epidemics," The Lancet, Vol. 12, April 2012, p. 275.

- Russia has the largest population of IDUs in the world an estimated
   1.8 million people.
- Over third have HIV; some regions much higher.
- Estimated 90% of Russian IDUs have hepatitis C
- Most patients co-infected with HIV and tuberculosis in Russia are drug-dependent.
- Majority of drug addicts are between 18 30 years old.
- Many a history of offending and commit a large number of crimes to finance their addiction.

Russia. US Department of State Bureau for International Narcotics and Law Enforcement Affairs, "International Narcotics Control Strategy Report: Volume I: Drug and Chemical Control (Washington, DC: March 2018)

- 2017 St Petersburg conference, experts reported that in 2016, there were 637,482 people incarcerated in Russia 63% for drug offenses, and 10% HIV positive.
- 54.5% Russian narcologists list religion as "the most suitable therapy" for drug addiction
- Drug addiction often treated with antipsychotic drugs, physical abuse
- Poor interagency and inter-sectoral cooperation, and lack of a cohesive national rehabilitation program.

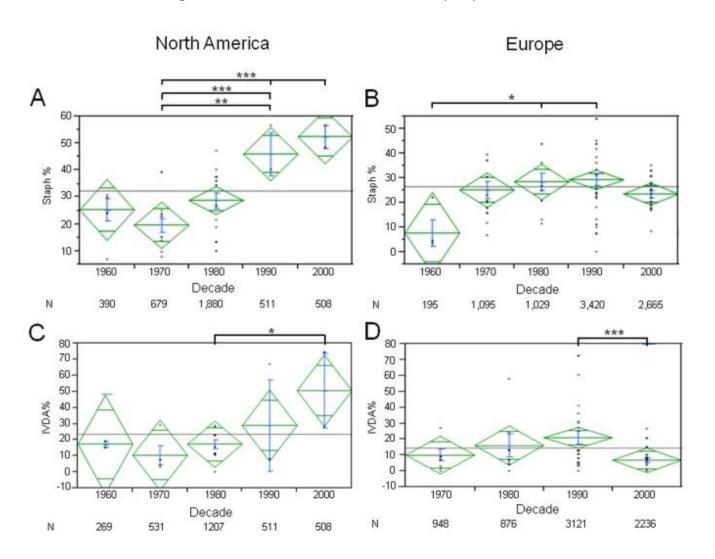
Russia Merkinaite, S. A war against people who use drugs: the costs. Eurasian Harm Reduction Network (EHRN), Vilnius: 2012, pp. 21-22. http://www.harm-reduction.org/...

- Russian Federal Drug Control Service has acknowledged, over 90% of drug treatment patients return to using within one year.
- Number of people living with HIV in Russia continues to rise
- 2010 58,633 new HIV cases were registered in the country.
- IDU predominant risk factor in 80% of all HIV cases

Global trends PWID. World Drug Report 2018. United Nations publication, Sales No. E.18.XI.9. https://www.unodc.org/wdr2018/

- Half of all PWID worldwide in 2016 estimated to reside in China, the Russian Federation and United States.
- 3 countries account for:
- 27% of the global population aged 15–64 years
- 45% of the world's PWID, an estimated 4.8 million people.

Infective Endocarditis Epidemiology Over Five Decades: A Systematic Review. Slipczuk et al. PloS One 2013. Regional Differences for Staphylococcus Aureus and Intravenous Drug Abuse.



(Staph, SA) IE in North America (A) or Europe (B) and intravenous drug abuse related IE in North America (C) and Europe (D), of patients in each decade.

N below decades represents total no. patients in each decade.

- A) SA increased markedly over last half century in N America
- B) No changes in SA were found in Europe.
- C) IVDA related IE frequency increased in North America.
- D) IVDA related IE percentage decreased in Europe in the last decade. \*= p<0.05; \*\*=p<0.01; \*\*\*=p<0.001.</p>

### Australia NSPs

- Established in 1986
- Aim preventing BBV by providing sterile injecting equipment free of charge.
- Services through funded primary NSPs, community health services, EDs, municipal councils, drug treatment agencies, youth organisations and participating pharmacies.
- 2009-2014 over 50 million needle and syringes distributed across Victoria by the NSP (average 10,854,026/year).
- 2014-2017 over 35 million needle and syringes were distributed (average 12,466,369/year).

# Summary IDU-IE

- IDU IE contributes 10-16% of all IE
- Predominantly S aureus increasing CA MRSA
- Increasing young white females
- Increasing hospitalisations, severe presentations and substantial HC costs
- High rates of recurrences IE OR 2.9
- Low mortality and good surgical outcomes
- Increasing in countries particularly with punitive policies
- Decreasing in countries with harm reduction strategies/chlorhexidine antisepsis
- Public health interventions are required to curb the increasing incidence of IDU IE.
- Increase education/improve access to sterile equipment and skin disinfection.
- Better addiction medicine support for in and outpatients may help reduce incidence of IDU IE.

# Acknowledgements to Geelong Endocarditis research team

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