The Opioid Epidemic – Iatrogenesis on a Global Scale

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Dr Chris Rumball
Dr Chris Hayes

ASB Theatre, Aotea Centre
Auckland, New Zealand

1.45pm-3.15pm
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Introductory Remarks

- Welcome everyone - we trust this session will be of great interest to the broad membership of our College, given the prominence of the clinical issues to be discussed
- In this session, I will begin by discussing the nature & scale of the opioid problem; what is going wrong & some of the clinical & system level changes that require our attention
  - **Dr Chris Rumball** will discuss the opioid crisis from the perspective of a pain specialist in NZ, evolving understanding of the neuroscience of pain & its implications for clinical management
  - **Dr Mat Brick** will share his personal experience & will put a human face to the 'frightening, lonely & dangerous disease of addiction'
  - **Dr Chris Hayes** will discuss the evidence & why the future for pain management might look quite different to the past & present
- Following these presentations we will open the floor for questions & discussion

Nature of the Problem

- Chronic noncancer pain is commonplace with an estimated prevalence of 15-20% (definitional differences) in both Australia & New Zealand

  –Delloite, 2019; sapere, 2019;

  –New Zealand National Health Survey (2016-2017)

- Opioid medicines are effective in managing acute pain, cancer pain, pain in palliative care & opioid dependence
  - –However, as we will discuss today, their clinical utility in the management of CNCP is an entirely different matter

Importance of Psychosocial Dimensions

- The importance of the psychosocial dimensions of chronic pain have long been recognised but in the cut & thrust of busy clinical practice, the treatment of pain has focused on prescribing medications & in particular, opioid medicines, rather than on addressing these broader dimensions that can alternatively modulate or exacerbate the perception, physical, emotional & functional responses to pain

- Understandably, CNCP may be associated with significant distress
  - We all recognise this can lead to maladaptive responses in the patient
  - Most worrisomely, this can also lead the patient's treating doctor to respond in an equally maladaptive, non-evidence informed manner

Nature of the Problem

- The world has witnessed a dramatic escalation in opioid prescribing since the turn of the Century, particularly in the USA, Canada, Northern Europe & Australia
- In 2016, overdoses provisionally accounted for 64,070 deaths in the USA
  - –A 21% increase over the preceding year & …
  - –With an est. 83% of these deaths involving an opioid
- The pharmaceutical industry has played a key role in this through marketing, strategically working to persuade the medical profession that strong opioids are effective & safe when prescribed long term for CNCP
  - –This has been associated with parallel increases in serious adverse events including rising overdose death rates, while clinical outcomes (analgesia, function & QOL) have not generally improved, contrary to patient expectations & industry claims

Billionaire founder of opioid firm guilty of bribing doctors to prescribe drug

John Kapoor, 75, also guilty of defrauding insurance companies
Prosecutors say fentanyl drug Subsys fuelled opioid epidemic

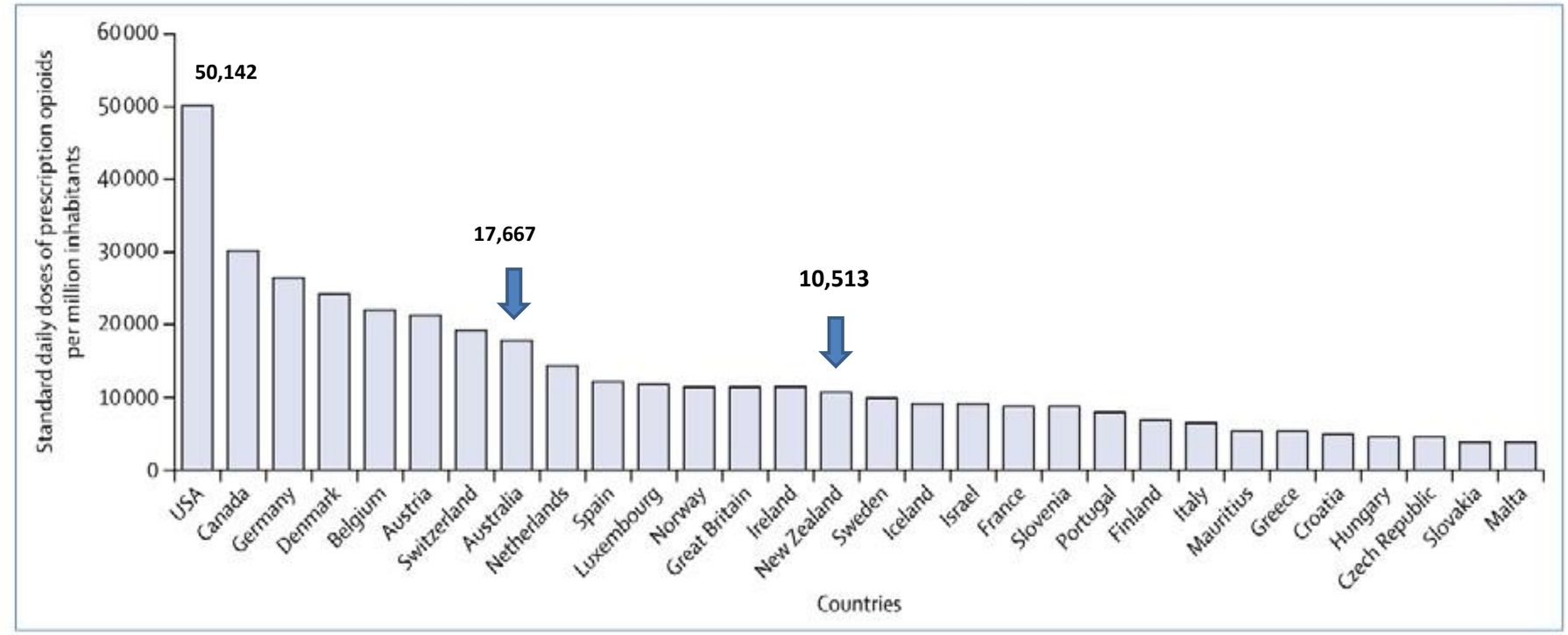
Chris McGreal *in Kansas City*

Thu 2 May 2019 20.17 BST

The head of a leading drug manufacturer has been found guilty of bribing doctors to prescribe a dangerous painkiller to patients who did not need it, in the first criminal conviction of a pharma chief over the opioid epidemic.

Where do we Stand on a Global Scale?

- On the basis of data provided by member states (daily divided doses or DDD), a UN report (2016) suggests that Australia is 8th on a league table of opioid consumption per million persons while New Zealand is 15th



Top 30 opioid-consuming nations, 2012–14 using DDD/million inhabitants/day. Source: United Nations International Narcotics Control Board, 2016 as cited in Humphreys (2017). This calculation includes buprenorphine, codeine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, pethidine, and other opioids.

Size & Seriousness of the Problem

- Of all the commonly used drugs, opioids have by far the highest mortality risk
  - Darke (2014) estimated that by the age of 50yrs, about half of any cohort of illicit opioid users will have died, with overdose being the most common cause
- The size & seriousness of this clinical & public health problem is highly visible in northern America as it is now in Australia & is quite understandably forcing a serious rethink within the medical profession
- While Australia is already treading in the footsteps of Northern America, NZ is not yet experiencing these problems to the same extent
- The pharmaceutical industry is now targeting many other countries of the world in its opioid marketing activity (‘*colonisation*’), further fuelling the global opioid epidemic
- New Zealand has the opportunity to avoid an opioid epidemic of similar proportions while at the same time, ensuring better quality pain management

Opioid Induced Deaths in Australia & New Zealand

- Analysis of the ***Australian*** National Mortality Database found that, in 2016, of 1,808 drug-induced deaths, more than **1,100** of these mentioned **opioid poisoning** (one or more times), up 89% from 591 deaths in 2007
  - Of opioid deaths in 2016 (AIHW, 2018):
    - 550 mentioned **other opioids** (includes prescription opioids such as oxycodone, morphine & codeine)
    - 361 mentioned **heroin**
    - 208 mentioned **methadone**
    - 234 mentioned **other synthetic opioids** (e.g. fentanyl & tramadol)

- In **NZ,** between **35 - 47 deaths/yr** were reported between 2009-2013
  - Between 2009 & 2013, there were 200 deaths in ***New Zealand*** attributed to 'narcotic or psychedelic drug poisoning' *(NZ Ministry of Health (2017)*
  - With the peak in 2012 & nadir in 2010
- Most of these are presumed opioid related

Deaths are considered "drug induced" if directly attributable to drug use (e.g. OD), & "drug related" where drugs played a contributory factor (e.g. MVA).

Unable to Demonstrate Effectiveness

- The US CDC & the Faculty of Pain Medicine (ANZCA) are among leading health bodies concluding on the basis of large systematic reviews & meta-analyses that there is ‘insufficient evidence to determine the effectiveness of long-term opioid therapy for improving chronic pain & function’
  - This is an astonishing finding given the colossal number of prescriptions written for these medicines globally, over the past several decades!
- At the same time, those reviews have revealed worrisomely high rates of wide ranging & serious adverse events & unwanted side effects:

- Respiratory
- CNS
- GIT
- CVS
- Endocrine
- Immune
- Hyperalgesia
- Fractures
- Depression
- Sleep quality

Defining Effective (Quality) Care

- Prescribing any medicine is difficult to justify where there are unclear clinical benefits, particularly in the face of obvious, common & serious adverse outcomes

- In its report *Addressing unwarranted variation: literature review on methods for influencing practice*, the Health Quality & Safety Commission New Zealand (2014) stated that **effective care is defined as interventions for which the benefits far outweigh the risks** (p.4)

Benefits Must Clearly Outweigh Serious Risks

evolve

evaluating evidence. enhancing efficiencies.

The Royal Australasian College of Physicians

- In modern day medicine, the community is entitled to expect that the medical profession would only consider prescribing a class of medicine with these kinds of serious adverse events if the treatment is highly effective, if there are no safer & better alternative medicines or treatments & if the risks & harms are justified by the good clinical outcomes
  - Once again, the evidence does not provide that reassurance, rather, it suggests that when prescribed long-term for CNCP, these are high risk/ low value medicines that can no longer be considered a centerpiece of chronic non-cancer pain management (FPM, 2015)
- Our college established the evolve initiative (led by specialists at the RACP) to **drive high-value, high-quality care** in Australia & New Zealand, while **disinvesting in low value care**

Closing the Evidence-Practice Gaps

- The question arises, why are so many among the medical profession continuing to prescribe opioids for CNCP in the face of poor clinical outcomes?
  - Are we routinely & ongoingly assessing benefit, risk & harm using a structured approach, for example, on the basis of universal precautions & the 5As + 2As framework & responding meaningfully & in a timely manner in our clinical actions?
  - Are we reliably diagnosing & responding appropriately to that assessment, including opioid dependence?
- As medical specialists, are we providing medical leadership in our clinical interactions with patients referred to us & in our advice to them & to the referring doctor?
- Are we advising or actively deprescribing in a timely manner where poor clinical outcomes ('treatment failure'), ongoing unacceptable risk & avoidable harms are evident, while also recommending more appropriate Rx?

1. **A**nalgesia	1. **A**dherence
2. **A**ctivity	2. **A**ccurate medical records
3. **A**dverse events	
4. **A**berrant behaviors	***5As + 2As Framework***
5. **A**ffect modulation	

Other Pharmaceutical Iatrogenesis

- We are also witnessing rising problems associated with other classes of medicines & there are common themes
  - Benzodiazepines, antipsychotics, anti-depressants, Gabapentinoids, psychostimulants…
- These medicines have psychotropic properties, may trigger reinforcing 'brain reward' pathways & alter the way people perceive, think (*cognition*), feel (*affect*) & behave
- Their prescribing is too often in irrational & unsafe combinations, doses & clinical contexts, signaling an apparent expectation or hope that a medicine will solve or enduringly relieve often complex health & human problems
- While many medicines do save lives, extend lives & improve QOL, the pharmaceutical industry has been only too pleased to promote 'the magic of pharma' in ways that are often unjustified by the evidence

Medicinal Cannabis Low Value/ High Risk Care (Pain)

"Effects suggest that number needed to treat to benefit is high, & number needed to treat to harm is low, with limited impact on other domains. It seems unlikely that cannabinoids are highly effective medicines for CNCP" (Stockings et al, 2018)

- I observe this is now playing out in relation to **medicinal cannabis** where quite extraordinary claims of therapeutic application & benefit are being promoted in the absence of sufficient if any high quality evidence of clinically meaningful effectiveness & safety & a new industry is gearing up to reap immense commercial rewards, regardless
  - The community does not know or understand the current evidence that the NNT = 24 for a 30% reduction in pain (a small effect), while the NNH = 6; & what this means (Whiting et al, 2015)
  - It does not appreciate that in Australia, it presently costs the healthcare system $576,000 for one person (in 24 treated) to achieve a modest benefit of 30% reduction in pain
  - In *evolve* terms & on the basis of current knowledge this this looks like another very low value-high risk 'medicine', particularly in relation to pain management

Medical Duty of Care Obligation

- The medical profession has a duty of care obligation to advocate for, provide or facilitate safe, good clinical care for patents experiencing CNCP
  - It also has a responsibility to avoid unwitting harm, including inappropriate supply of pharmaceuticals to the illicit market & potentially contributing to the spread of opioid dependence in the community
    - In Tasmania, up to 30% of all prescribed morphine (by weight) is diverted to IDU (NDARC, 2012)
- In reference to iatrogenic harm, in his inquest findings in 2016, Tasmanian Coroner Stephen Carey sent a clear & strong message to the medical profession when he referred to an opioid overdose death as **'likely & avoidable'** rather than an 'accident'
- Clinical care is hardly compassionate care if it is low value & if it commonly causes serious harm

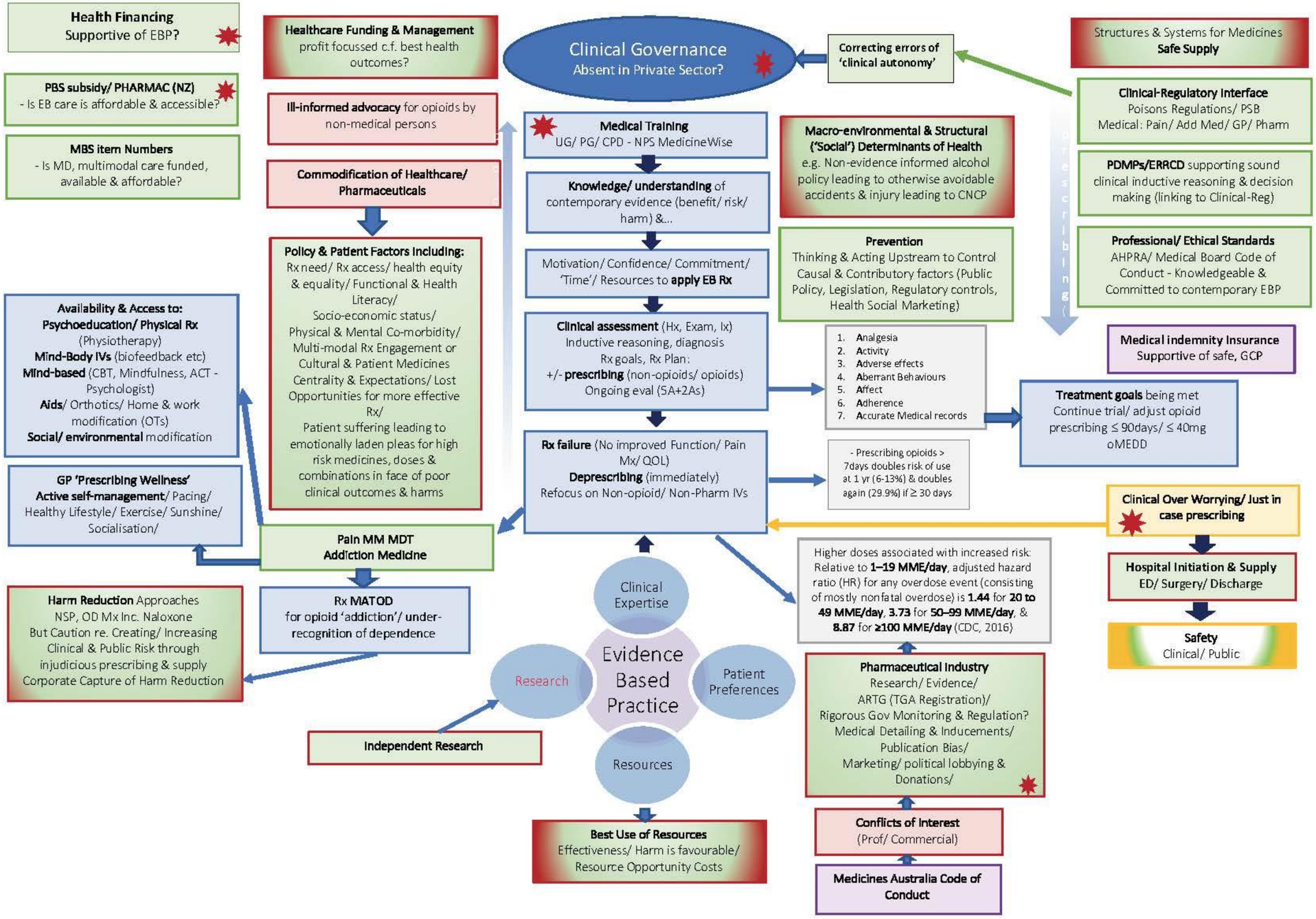
Drug Dependence No Small Matter

- In my clinical & clinical-regulatory roles I observe that many GPs & pain specialists in Australia continue to miss obvious ‘red’ & ‘yellow’ flags, miss the diagnosis of opioid (& other drug) dependence & thereby provide sub-optimum & unsafe treatment (though I also evidence of improvement)
  - –As Mat Brick will share, ‘Addiction’ is no small matter
- **Drug dependence** to any substance characteristically diminishes an affected person’s life opportunities, life chances & life course
  - –It axiomatically diminishes their ability to freely make & to act on good choices, live a full life & flourish to the maximum of their potential.
  - –It diminishes their autonomy & human agency
    - Though thankfully people can & do come through this with good support & care

New framework for assessment of dependence - ***ICD-11*** (WHO, 2019):

1. *Impaired control over substance use*
2. *Substance use is a priority in life*
3. *Physiological features*

Factors Influencing Translation of Evidence into Medical Practice



Against the Odds, Physicians can make a Difference

Notwithstanding all the perverse incentives & structural impediments that may weigh against good clinical care, even if we fail to look & act upstream in the chain of causation of clinical outcomes, the **prescription pad** & the **pen** that inks the **letter** back to the referring GP rests in our hands

While noting the complex array of factors influencing life chances (e.g. *first 1,000 days of life'*), Fellows of the RACP can bring the *evolve* initiative alive by leading change across this broad array of factors impacting the application of evidence & in their own clinical practice