# UPDATE ON ADDICTION PRIMARY CARE

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### Overview

- Policy and political update
  - Cannabis
  - Gaming and internet
  - Alcohol protecting public health or protecting the alcohol industry? vested interests, minimum pricing
- New/old/unusual patterns of use
- Testing advances
- Alcohol treatment matching the intervention to the severity
  - Screening, and brief interventions
  - Abstinence promoting medications post detoxification
- Benzodiazepines, Pregablin; Anxiety and Sleep
- Unintended Prolonged Opioid Use UPOU
- Complex comorbid issues COPD
- Case studies including Inquest Case
- Q and A

### Scale of the problem

Substance problems continue to evolve



Rview May 2018 Addiction, looked at global burden of death and disease from alcohol, tobacco and illicit drugs.

Global estimates 1 in 7 15.2% smoke, 1 in 5, 20% heavy alcohol use

Western, Eastern, Central Europe highest alcohol consumption per capita (11.09, 11.98, 11.61 litres per head respectively)

2015 annual global human cost alcohol and tobacco was 1/4 billion disability adjusted life years

Illicit drugs tens of millions Death rates internationally increasing for opiate related deaths

#### Impact on society

- Annual cost in in region of UK £20 billion and in US \$300 billion
- Estimates that 1 million children in UK with at least one parent are consuming more than 7.5 units alcohol daily
- 350,000 cases of domestic violence are alcohol related
- Alcohol related liver transplantation rates have increased
   5 fold since 2002
- Industry revenues made from alcohol/gambling continue to influence and impact government policy
- Problems of the online availability 24/7 for behavioral addictions

### Substance addictions

- Alcohol
- Opiates eg heroin, morphine, OTC
- Cocaine and other stimulants amphetamines
- Ecstasy and MDMA
- Hallucinogenics eg LSD, magic mushrooms psilobilin
- Novel substances: mephedrone, miaow-miaow, mcat, bath salts, GBL gamma-Butyrolactone, rohypnol, ketamine
- Anabolic steroids

#### **Behavioural addictions**

• Gambling, internet, shopping, sex and love addiction, food



### **Policy Updates**

- Cannabis
- Gaming
- Sex addiction now on DSMV
- Cryptomarkets
  - online anonymous vendor using bitcoin
  - new channel for global drug distribution
  - able to evade prohibitive controls, customs not able to intercept all post
  - Cryptomarket drug trade increasing sales tripled from Sept 2013
  - Revenue estimated in US at \$14 mill per month in 2016

### Cannabis

- Home secretary Sajid Javid announces new review into medicinal cannabis but rules out legalizing the drug
- ? Policy shift associated with increasing use and reduced perception of harm and calls for decriminalization
- (Azofeifa et al 2016)
- Growing evidence that earlier onset, greater intentsity of use are associated with increased occupational, social and psychological problems (*Levine et al 2014, Volkow et al 2016*)
- Interest in cannabis oil -but difficult to define what its actual composition is

# Gaming NHS Clinic

- Gambling clinic expanded to including gaming online
- Will accept national referrals subject to criteria
- Address: 69 Warwick Road, London SW5 9BH
- Tel: 0207 381 7722
- Fax: 0207 381 7723
- Email: gambling.cnwl@nhs.net

# Why do people use?

- Not just a search for fun?
- Pleasure seeking reason reported in less than 20% of addiction sufferers
- Many self medicate for anxiety, depression, pain, trauma, boredom, anger
- Common associations:
- Social anxiety benzodiazepines
- Internet adolescent ASD spectrum, 'failure to launch'
- ADHD (Attention Deficit Hyperactivity Disorder) stimulants cocaine, amphetamine
- Depression cocaine and alcohol misuse (which then worsens the condition longer term)
- Confidence cocaine often seen in sales jobs
- Reduction of pain or boredom opiates
- Search for meaning or psychedelic experience hallucinogens LSD
- Not always static some do start for pleasure then continue to avoid withdrawals

# GBL (Gamma- butyrolactone)

- GBL precursor of GHB (gamma hydroxy butyric acid)
- Clear liquid used in club scene in London, metabolised within 24 hours
- Similar to Rohypnol in properties
- Naturally occurring in spine
- Euphoric effect at low doses, promoting confidence but sedative at higher dosages
- High risk of toxicity with confusion with nystagmus, aggression, urinary incontinence and nausea with toxicity
- Severe withdrawal if stopped suddenly
- Needs specialist inpatient detoxification with very high dosages of Diazepam
- Average dose of Diazepam required in detox in recent study was 335mg

### Ketamine

- Used as veterinary anaesthetic
- Special 'K'
- Used as euphoric substance but really 'dissociative' anaesthetic
- Produces trance like state while providing pain relief and memory loss
- Urinary complications with irreversible bladder damage
- Due to fibrosis

#### Mephedrone

- 4 Methylmethcathinone amphetamine like substitute
- Rapid increase in use over last few years
- Recently became illegal but was named legal highs
- 'Bath salts', MCAT Miaow Miaow, Topcat
- Oral or injectable
- Euphoria, perspiration, increased libido but idiosyncratic psychiatric effects such as psychosis



KETAMINE HE

For Intramuscular Use Store at controlled room temperature 15° to 30°C (59° to 86°F). Protect from light. DOSAGE: See package insert. For use in cats and

subhuman primates only.

Not more than 0.1 mg/mL benzethonium chloride added as a preservative.

Color of solution may vary from colorless to very slightly yellowish and may darken upon prolonged exposure to light. This darkening does not affect potency. Do not use if



### LSD and the psilocybins

- Lysergic acid diethylamide
- Hallucinogenic
- Used in some cults to promote unity



- 1960s Timothy Leary psychology academic Harvard experimented with them to enhance creativity in art and music
- Aldous Huxley Doors of Perception, Burrows the Naked Lunch etc
- Recent reports from Arizona of Colorado river frog licking its back and hallucinergic effects

#### Anabolic steroids

- Driven by athletic performance or dissatisfaction or need to obtain muscular physique
- Abused in cyclical fashion 4-18 weeks on with one months to a year off
- Oral and injectible combined
- Often use other drugs
- Side effects: aggression; MI; hepatic; injection risks, gynaecomastia

#### Drug detection windows in urine analysis

- Cannabis
- Cocaine
- Opiates
- Amphetamines
- Benzodiazepines
- GBL Rohypnol

5-30 days 2-3 days 4-10 days 2-4 days 3-30 days 24 hours

## Saliva

#### Advantages

- Simple, hygienic
- Easy to store/transport
- No undignified supervision
- Immediate results
- Difficult to falsify
- Disadvantages
- Serial testing required
- Difficult to take adequate sample
- Only short window of detection days/weeks covered
- More research needed to clarify accuracy



### Sweat tests

Advantages



- Window of detection longer can be worn for up to a week and in situ
- Can be used as monitor for adherence to treatment and veracity of self report
- Becoming more common in family proceedings to monitor parental compliance with orders
- Disadvantages
  - False positives a problem skin contamination possible
  - Narrow number of drugs identified cocaine, opiates,
  - cannabis
  - Less established research base
  - Fingerprint perspiration study University of Surrey
    - in progress



#### Alcohol

#### Major Public Health concern

- 10% population alcohol dependent USA and Europe
- 8 in 10 in Europe and Americas will report drinking in lifetime
- Starting age USA 14yrs (average)
- Culturally increasingly more acceptable across cultures
- Increasing numbers of women and higher prevalence of FAS
- 1 in 7 will become dependent
- Significant morbidity and mortality-rates of alcoholic hepatitis leading to cirrhosis and requiring liver transplantation have increased approximately 5 fold in last 5 years
- Screening and Brief Interventions
  - Screening followed by 5-30 min intervention (AUDIT; CAGE; SIPS;FAST)
  - Very effective in primary care WHO, Wallace et al 1 yr f/up
  - Some studies say at least as effective as intensive specialist interventions

#### Effects of high risk drinking

#### **Effects of High-Risk Drinking**



High-risk drinking may lead to social, legal, medical, domestic, job and financial problems. It may also cut your lifespan and lead to accidents and death from drunk en driving.

# New alcohol research focus moving to shared responsibility

- Overly individualized approach in evaluation of research methods rooted in rational thought and social cognition
- Meier at al alluded to 'victim blaming' culture in paper <u>"All</u> drinking is not equal" https://doi.org/10.1111/add.13895
- Individual over time may be able to reduce or stop consumption
- However it is essential to also change institutional structures that allow easy access to alcohol;
- Intense marketing and promotion from the alcohol industry false marketing for cancer prevention (Mart et al 2012)
- Requires political and community support and effective policies such as minimum pricing now in operation in Scotland

### Key to terms

#### Alcohol dependence

#### · 3 or more symptoms in the last year

- · Compulsion or desire to use
- Problems controlling use; onset, termination, levels
- Withdrawal state
- Tolerance
- Neglect of interests
- · Persisting with use despite harm
- Also craving, and rapid reinstatement
- Mild score of 15 or less on SADQ (Severity of Alcohol Dependence Questionnaire)
- Mod score of 15-30 on the SADQ
- Severe score of 31 or more on the SADQ

#### Harmful drinking

- A pattern of consumption causing medical or psychiatric problems eg acute pancreatitis, depression, accidents
- Often accompanied by significant social harm such as marital breakdown, unemployment
- Hazardous drinking
  - A pattern of consumption that increases the risk of harm

#### Box 4

#### Audit

#### The Alcohol Use Disorders Identification Test: Interview Version

Read questions as written. Record answers carefully. Begin the AUDIT by saying "Now I am going to ask you some questions about your use of alcoholic beverages during this past year." Explain what is meant, by "alcoholic beverages" by using local examples of beer, wine, vodka, etc. Code answers in terms of "standard drinks". Place the correct answer number in the box at the right.

How often do you have a drink containing alco- hol?     (0) Never [Skip to Qs 9-10]     (1) Monthly or less     (2) 2 to 4 times a month     (3) 2 to 3 times a week     (4) 4 or more times a week	6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?     (0) Never     (1) Less than monthly     (2) Monthly     (3) Weekly     (4) Daily or almost daily
<ul> <li>How many drinks containing alcohol do you have on a typical day when you are drinking?</li> <li>(0) 1 or 2</li> <li>(1) 3 or 4</li> <li>(2) 5 or 6</li> <li>(3) 7, 8, or 9</li> <li>(4) 10 or more</li> </ul>	<ul> <li>7. How often during the last year have you had a feeling of guilt or remorse after drinking?</li> <li>(0) Never</li> <li>(1) Less than monthly</li> <li>(2) Monthly</li> <li>(3) Weekly</li> <li>(4) Daily or almost daily</li> </ul>
<ol> <li>How often do you have six or more drinks on one occasion?</li> <li>Never         <ol> <li>Less than monthly</li> <li>Monthly</li> <li>Weekly</li> <li>Daily or almost daily</li> <li>Skip to Questions 9 and 10 if Total Score for Questions 2 and 3 = 0</li> </ol> </li> </ol>	8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?     (0) Never     (1) Less than monthly     (2) Monthly     (3) Weekly     (4) Daily or almost daily
<ul> <li>4. How often during the last year have you found that you were not able to stop drinking once you had started?</li> <li>(0) Never <ul> <li>(1) Less than monthly</li> <li>(2) Monthly</li> <li>(3) Weekly</li> <li>(4) Daily or almost daily</li> </ul> </li> </ul>	9. Have you or someone else been injured as a result of your drinking?     (0) No     (2) Yes, but not in the last year     (4) Yes, during the last year
5. How often during the last year have you failed to do what was normally expected from you because of drinking?     (0) Never     (1) Less than monthly     (2) Monthly     (3) Weekly     (4) Daily or almost daily	<ul> <li>10. Has a relative or friend or a doctor or another health worker been concerned about your drinking or suggested you cut down?</li> <li>(0) No</li> <li>(2) Yes, but not in the last year</li> <li>(4) Yes, during the last year</li> </ul>

### AUDIT

- A score of 8 or more is associated with harmful or hazardous drinking
- Score of 13 or more in women, and 15 or more in men, is likely to indicate alcohol dependence
- Assume higher risk to those with similar scores but who are more vulnerable to the effects of alcohol eg elderly, women

#### Audit

- Risk Level Intervention AUDIT score\*
- Zone I Alcohol Education 0-7
- Zone II Simple Advice 8-15
- Zone III Simple Advice plus Brief Counselling
- and Continued Monitoring 16-19
- Zone IV Referral to Specialist for Diagnostic 20-40
- Evaluation and Treatment
- \*The AUDIT cut-off score may vary slightly depending on the country's drinking patterns, the alcohol content of standard drinks, and the nature of the screening program. Clinical judgment should be exercised in cases where the patient's score is not consistent with other evidence, or if the patient has a prior history of alcohol dependence.

# Sips

#### TO BE COMPLETED BY CLINICAL STAFF Screening procedure

For the following question - 1 standard drink = 1 unit of alcohol. An indication of standard drinks is provided in the diagram below.

Г

	-	One	Standard Drin	ik (si	
		n of These. T small gran		giess of	Tangie measure
	The following	quantities of alc	ohol contain	more than 1	standard drink
	2 Canad Amateria				
6	Do you feel your	attendance here is	related to your	drinking [	Yes (PAT +ve)
	Pisase place a c	ross in the releva	nt box.	[	No (go to Q2)
•	MEN: How o WOMEN: H	often do you have t low often do you ha	DGHT or more we SIX or more	standard drinks standard drink	a on one occasion? a on one occasion?
	Never	Less than monthly	Monthly	Weekty	Daily or almost daily
	patient's respons	e is "Monthly", or "M	Veekly', or 'Dail	y or almost daily	y they are PAT+ve.
the lease	e indicato the res	uit of the screening	g procedure by terminate the i	Positive	In the appropriate box Negative
the lease the the ique	e indicato the res , result is negative collected by rese result is positive at written consen	uit of the screening a thank the patient, and staff. explain the study t	g procedure by terminate the i o the patient, p	placing a cross Positive	In the appropriate box Negative one the survey securely nation sheet and
the elow the que	e indicate the res result is negative collected by rese result is positive at written consen patient willing to	uit of the screening a thank the patient, arch staff. explain the study t f. provide written info	g procedure by terminate the i to the patient, p vmed consent?	placing a cross Positive provide an inform Yes	In the appropriate box Negative one the survey securely nation sheet and No
the elow the obe the ique the yes	e indicate the res result is negative collected by rese result is positive at written consen patient willing to continue with the	uit of the screening a thank the patient, and staff. explain the study b t. provide written info i consent details ov	g procedure by terminate the i to the patient, p inned consent? refeat.	placing a cross Positive Interview and sto rovide an inform	In the appropriate box Negative one the survey securely nation sheet and No
f the Pleas below f the o be f the eque s the f yes f no t	e indicate the res result is negative collected by rese result is positive at written consen patient willing to continue with the eminate the inte mber to provide 1	wit of the screening a thank the patient, arch staff. explain the study t t. provide written info i consent details ov rview and store the the patient with a P	g procedure by terminate the i to the patient, p primed consent? refeat. survey secure stient informati	placing a cross Positive interview and sto rovide an inform Yes Yes iy, to be collects on Leaflet.	In the appropriate box Negative one the survey securely nation sheet and No No

#### SEVERITY OF ALCOHOL DEPENDENCE QUESTIONAIRE (SADQ-C)1

$C \wedge D \cap$	NAME			AGE	No
SADQ	DATE:				
	Please recall a typica	l period of heavy drink	cing in the last 6 r	nonths.	
	When was this? Mor	11h:			
	Please answer all the appropriate response.	following questions al	bout your drinking	g by circling	your most
	During that period	of heavy drinking			
	<ol> <li>The day after dri ALMOST NEVER</li> </ol>	nking alcohol, I woke SOMETIMES	up feeling sweaty OFTEN	NEARL	Y ALWAYS
	<ol><li>The day after dri ALMOST NEVER</li></ol>	nking alcohol, my han SOMETIMES	ds shook first thin OFTEN	g in the mon NEARL	ning. Y ALWAYS
	<ol> <li>The day after drinking alcohol, my whole body shook violently first thing in the morning if I didn't have a drink</li> </ol>				
	ALMOST NEVER	SOMETIMES	OFTEN	NEARL	Y ALWAYS
	<ol> <li>The day after dri ALMOST NEVER</li> </ol>	nking alcohol, I woke SOMETIMES	up absolutely dre OFTEN	nched in swe NEARL	at. Y ALWAYS
	5. The day after dri ALMOST NEVER	nking alcohol, I dread SOMETIMES	waking up in the OFTEN	morning. NEARL	Y ALWAYS
	<ol><li>The day after dr morning.</li></ol>	rinking alcohol, I was	frightened of n	secting peop	e first thing in the
	ALMOST NEVER	SOMETIMES	OFTEN	NEARL	Y ALWAYS
	<ol><li>The day after dri ALMOST NEVER</li></ol>	nking alcohol, I felt at SOMETIMES	the edge of despa OFTEN	ir when I aw NEARL	oke. Y ALWAYS
	<ol> <li>The day after drin ALMOST NEVER</li> </ol>	nking alcohol, I felt ve SOMETIMES	ry frightened whe OFTEN	n I awoke. NEARL	Y ALWAYS
	<ol><li>The day after drin ALMOST NEVER</li></ol>	nking alcohol, I liked t SOMETIMES	o have an alcohol OFTEN	ic drink in th NEARLY	e morning. Y ALWAYS
	<ol> <li>The day after dri quickly as possib</li> </ol>	inking alcohol, I alwa le.	ys gulped my fir	st few alcoho	olic drinks down as
	ALMOST NEVER	SOMETIMES	OFTEN	NEARLY	YALWAYS
	<ol> <li>The day after drin ALMOST NEVER</li> </ol>	sometimes	more alcohol to g OFTEN	et rid of the s	shakes. Y ALWAYS

<sup>&</sup>lt;sup>1</sup> Stockwell, T., Sitharan, T., McGrath, D.& Lang, (1994). The measurement of alcohol dependence and impaired control in community samples. Addiction, 89, 167-174.

### **Brief Interventions**

- Advantages of interventions in primary care:
  - Patients with alcohol misuse tend to consult GPs more frequently than other patients
  - Early identification of excessive drinkers more likely to benefit than severely dependent patient with STM/ cognitive decline
  - Primary care seen as less stigmatizing than specialist clinic
  - No specialist training required
  - Time and cost effective

### **Brief Intervention - FRAMES**

- F –feedback about personal risk or impairment
- R emphasise personal **responsibility** for change
- A advice to cut down or if dependent, abstain
- M menu of alternative options for changing drinking pattern
- E empathic interviewing
- S self efficacy, interview style that enhances this
  - MENU Style Options Available:
  - Diaries to look at current consumption.
  - Limit no of days of drinking. 3-4 alcohol free days in week
  - Reduce strength of drinks and rate of consumption
  - Soft drink chasers after each alcoholic drink. Order water with wine. Dilute spirits.
  - Awareness of triggers to drinking boredom, stress, anger and using alternative strategies
  - Monitor LFTs especially GGT

## Abstinence or 'controlled drinking'

- Hazardous/harmful consumption and occasional risk free drinking
  - Success more likely with good social support; no impulsive personality traits
  - Advised if drinking is less than 1 year duration and no dependence features. Need at least 6/12 abstinence before controlled drinking starts.
- Abstinence is the only recommendation for dependent patients
  - Lack of control already established and unlikely to be regained
  - Rapid reinstatement
  - Beware of the unmotivated patient and collusions with 'cover up' rationalisations "I can't sleep without a drink Doctor",
  - "I can't function socially without one"

#### Potential pitfalls with enzyme induction and interactions

- Alcohol is metabolised by the same liver enzymes
- (CYP2E1) as paracetamol, phenobarbitone
- (CYP3A4)Benzodiazepines,Carbamazapine,Mirtazepine,Venlafaxine, Clozapine.
- In chronic drinkers enzyme induction can induce up to 10 fold increase in enzyme activity leading to problems with heavy binge/episodic drinkers:
- Reduced levels of medication when sober but when intoxicated medication competes with alcohol for liver enzyme metabolism and levels increase – risk of toxicity
- Medications that inhibit alcohol metabolism: Aspirin, H2 antagonists, Isosorbide dinitrate
- Cross tolerance with opiates. Often opiate users will drink if chosen illicit opiate not available
- Synergistic effect of opiates, alcohol and benzodiazepines respiratory depression and fatality risk at low dosages when used in combination. COPD case

#### Medically assisted withdrawal

- O/P managed withdrawal safe for mild to moderate alcohol dependence DTs/ fits / serious Psych Hx need I/P
- Fixed dose 30mg or 25mg Chlordiazpoxide q.d.s reducing to zero over 7 to 10 days. Ongoing strong vitamin B and thiamine 100 -300mg cover. Pabrinex in vulnerable cases
- Home and Ambulatory now only available at I Access,
- IP located at Bridge House Maidstone Kent Dr Annie McCloud
- GGT, LFT synthetic enzymes, amylase, platelets trajectory determine whether gastroenterology assistance is required
- LFTs very useful pre-assessment; for monitoring progress, post detoxification. 2-3 monthly even if well and to avoid medico-legal cases(!)
- Much better outcomes if motivated to engage with structured aftercare programme I Access RPG, Recovery Café, Catalyst, AA, SMART
- Kindling effects also with repeated detoxifications.

#### Abstinence promoting medications

#### Acamprosate Calcium

- best longstanding evidence for abstinence glutamate receptor
- Anti –craving effects
- 666mg t.d.s. if weight is over 60kg
- 333mg t.d.s. of under 60kg
- Check LFTs 2-3 monthly
- 10% have side effects such as diarrhoea, nausea, rash. (probably dose related)

#### Baclofen

- 30-60mg
- Safer excreted by renal system
- Good for people that drink to self medicate anxiety
- Naltrexone
- Opiate receptor antagonist also used for abstinence in opiate free individuals
- 50mg o.d. check LFTs 2-3 monthly
- Can increase agitation
- **Nalmefene** weak evidence from Fitzgerald at al 2016 Addiction 111;1477

#### Acamprosate calcium

- Acamprosate should not be used in the following circumstances:
- In pregnant or breastfeeding woman.
- In severe renal insufficiency (serum creatinine < 120 micromoles/L).</li>
- In severe hepatic failure (Childs-Pugh classification C).
- Licensed for use for 12 months
- Can be stopped abruptly

#### Baclofen

- GABAB receptor agonist gamma-aminobutyric acid agonist approved to treat spasticity.
- Preclinical work in rats reduces alcohol seeking behaviour, intake amounts and motivational cues.
- Human studies RCTs show safety and efficacy to reduce cravings and intake and promote abstinence. 30mg -60mg o.d.
- Single case studies with higher dosages 140mg and above also show benefit but not in BNF
- 15% metabolized by liver
- Can be used whilst drinking to see if intake reduces.
- Ref 2011 Alcohol and Alcoholism Vol 46 No 3 pp 312-317

#### Antabuse - Disulfiram

- Supply problems
- 200-400mg od
- Prevents alcohol dyhydrogenase metabolism of alcohol
- Effective and used in family proceedings to monitor progress and adherence with Court orders
- Problems with reliance on patients to take it
- Can supervise with agreement with pharmacy in some cases

### **Anxiety Disorders**

- · Common, disabling, under recognized, undertreated
- Female/ male ratio -3/2
- Work up FBC, ESR, UE, Thyroid function

#### Generalised Anxiety Disorder

- Panic Disorder
  - Bimodal age onset 15-24 yrs and 45-54 yrs.
  - Triggered by illness, injury eg surgery, interpersonal loss
  - Substance triggers: cannabis, caffeine, decongestants, cocaine, stimulant drugs
  - · Sertraline can induce panic
  - · SSRI discontinuation syndrome can induce symptoms similar to panic
- PTSD
- OCD
  - Strongly genetic.
- Social phobia
  - The most common, tends to begin before 20 years
- Specific phobia eg agoraphobia, arachnophobia, claustrophobia

# Treatment: pharmacotherapy and psychological

- · CBT, cue exposure, mindfulness, relaxation therapy IAPT
- Online CBT 'fear fighter' recommended by NICE, NIH.
- Ist Line: SSRI : Escitalopram, Sertraline or Citalopram go
- In addition: Propranolol XL 80 mg o.d. To combat physical anxiety symptoms
- Mirtazepine and Pregablin more sedating
- 2<sup>nd</sup> line: Venlafaxine XL 75mg o.d. or Duloxetine 30mg od less sexual side effects
- Pregablin very useful when insomnia or sedation needed and used in addition to AD
- Alprazolam and Clonazepam indicated for panic but not advised at all in those with dependence potential. Pregablin good alternative 25mg od.
- Benzos best reserved for refractory uncontrolled panic for short term specialist use.

#### Benzodiazepines and the anxiety axis

- Benzodiazepine misuse still significant problem and problem worsening especially with online 24/7 access
- Often self medication of undiagnosed anxiety disorders common and to heighten euphoria from heroin use or to cushion withdrawal from cocaine.
- 'Doctor shopping' and diversion to black market common.
- Rise of benzos occurred in 1960-1970 followed the replacement of toxic barbiturate sedatives
- Mid 1970's regulatory bodies recognised abuse potential of benzos even in therapeutic doses
- Dependence well described in early in drug development literature but oddly did not appear in medical literature until 1980's
- Late 1980's reports of intravenous abuse of gel filled temazepam

#### Benzodiazepine dependence

- Longer acting (diazepam) better than shorter (lorazepam)
  - Triazolam, short acting benzo for insomnia was withdrawn from British market following severe rebound anxiety after a single dose
  - Benzo detoxifications transfer all 'pams 'to diazepam before reduction
- Prescriptions longer than 8 weeks risk of inducing dependence
- Explain that benzo will exacerbate anxiety with long term use
- Treat all anxiety disorders *without* a benzodiazepine

### Benzodiazepine Conversion Table

Drug	Dose
Chlordiazepoxide	15mg
Diazepam	5mg
Lorazepam	500 micrograms
Nitrazepam	5mg
Oxazepam	15mg
Temazepam	10mg
Zalepron	10mg
Zopiclone	7.5mg
Zoplidem	10mg

## Sleep and the Z drugs

- Z drugs (zopiclone, zolpidem, zalepron) originally mis-sold as non dependence making
- Benefit of the Z drugs is that they do preserve normal sleep architecture. Benzos do not.
- Can iduce depednece after months of use so treat many as if benzodiazepine dependent
- Sleep significant issue. Alcohol, anxiety, depression conditions will affect sleep pattern themselves. Best to treat root cause first with least addictive options. Substitute with Pregablin, Mirtazepine, Trazadone
- Sleep hygiene advice crucial:
- Wake the same time each day, no cat napping at all
- Ask re caffeine intake no more than 2 cups coffee or 3 teas in day and not after midday.
- Morning light, effect of blue light on resetting circadian rhythm and Meltaonin axis No screens 2 hours before bed

#### Unintended Prolonged Opioid Use (UPOU)

- Non medical use of prescription opioids remains a public health crisis, where appropriate short term analgesia extends in some cases to indefinite extended prescriptions
- Most opioids prescribed by non pain specialists
- Urgent need to better understand UPOU
- Hooten et al Dec 2017 Mayo Clinic Proc 2017;92 (12);1822-1830 " A Conceptual Framework for Understanding Prolonged Opioid Use."
- Characteristics associated with transition to indefinite use:
  - Patient
  - Prescriber
  - Practice Environment

### Patient factors with UPOU

#### Medical Conditions

- Pulmonary and Heart Disease
- Diabetes
- Musculoskeletal
- PTSD
- Depression
- Smoking
- Substance Use
- Pain Etiology
  - Postoperative elective 8% opioid naïve still using after 90 days and 13% naïve still at 6-12/12
  - Trauma related surgery approx 1/3 still using opioids 3-4 /12 after surgery
- Individual Responses to Pain
  - Negative affect catastrophizing style higher doses needed
  - Pain perception and pain related anxiety
  - Variability in opioid analgesia genetic factors at u opioid receptor
- Sociodemographic Factors mixed
  - Female, age over 50 years, higher educational level, economic and unemployment unknown

Chronic Pain Chronic Pain Chronic Pain

#### **Prescriber and Practice factors UPOU**

- More conservative prescribing noted in those who had:
- access to specialist advice, and CPD
- online training course in opioids and pain management
- enhanced regulatory environment Florida then Texas state implemented laws to curtail proliferation of opioid clinics
- Other factors which influenced prescribing style include:
  - Personal beliefs and attitudes
  - Incentives from insurance and other funding

### **Opiates and pain**

Opioid crisis for chronic pain BMJ

Dhalla IA, Persaud N, Juurlink DN Facing up to the prescription opioid crisis BMJ 2011; 343:d5142 (23<sup>rd</sup> August 2011)

#### Dos and Don'ts:

- 1. Be familiar with national and international guidelines on strong opioids in chronic pain
- 2. Not all patients respond to opiates. If side effects are greater than benefit then reduce and stop them.
- Set limit to maximum dose. 'Ceiling effect' in chronic pain of 10-30% reduction of pain
- 4. Consider restricting who prescribes long term opiates for pain to experienced clinicians
- 5. Do no prescribe more than one opioid to an individual patient long acting formulations are preferable
  - Brisitsh Pain Society. The British Pain Society's opioids for persistent pain:good practice 2010 <u>www.britishpainsociety.org/book\_opioid\_main.pdf</u>.

#### Current issues with opiates

- Shared care joint advice clinics initiative needed using Pain and Addiction Expertise
  - Request had gone for funding to the CCG for this
- Supply problems with Buprenrophine, Lofexidine ongoing
- Extended release Naltrexone SR- NTX
  - Saxon et al 2018
  - Effective in clinical practice for prevention of relapse to opioid dependence

#### Inquest Review - Case 1

- Patient chronic COPD and past Heroin injector, back injury on Codeine from GP tolerant to Methadone at time of death with no illicit opiate use
- Rx Physpetone 40mg SP died after effective Methadone treatment but after suffering respiratory arrest
- Frequent chest infections months prior to death but presented with loss of weight over several weeks prior to death - no acute SOB
- Opiate poisoning was surprising initial COD by pathologist triggering Inquest
- SP had moved from injecting to smoking then stopping Heroin use stabilizing on reducing regime of 40mg Methadone at death. Max ever dose was 55mg
- Evidence at Inquest revealed that symptoms of respiratory arrest minutes before collapse were not indicative of Methadone poisoning
- No TDP 'torsades de pointes' or depressed drive to breathe from paramedics at final attendance.
- Pathologist revised initial COD of 1'Methadone poisoning after hearing evidence of elevated CRP and bradycardia prior to death but still wanted Methadone as 2' COD
- Coroner eventually disregarded this and listed as COD as Natural Causes but raised need for close communication between 1 and 2 care due to knife edge existence for those with COPD and risk of exacerbations and fatality
- Raises complexity of managing this patient group.
- Reduce Physpetone or opiates during exacerbations?
- Limit all respiratory depressants including benzos?

# Case study 2 – OTC, back pain and Migraine

- Solicitor works 12 14 hour days with regular over night work sessions. Anxious about workload and poor back
- Medicated for his back ache and stress induced migraines with codeine OTC. As workload increased so did migraines
- Dealing with very high level stress in job and needed to perform
- Unable to take time off 'presenteeism'
- Culture of firm a problem felt he could not take time off
- Codeine became out of control and developed physical dependence syndrome
- Stopped codeine by transferring to Buprenorphine
- Back pain alleviated by firm purchasing standing table
- Now stable on Buprenrophine 2mg

### Case 3 - OTC

- 45 yr old man, IT specialist, fitness obsessive, sole carer to three teenage daughters
- No previous psychiatric or medical history
- Injured back during weight lifting. Tried various conservative options to combat pain but found that OTC codeine /paracetamol effective.
- Didn't want to bother any medical professionals
- Over 4-6 weeks control of therapeutic dosage lost.
- Increasing no of tablets taken. Often would wake in night to drive to late night chemist to obtain codeine medications
- Discovered OTC morphine preparation. Crisis when ran out of morphine and took 57 codeine/paracetamol tablets to avoid opiate withdrawals. Needed assessment in A&E for OD possibility.
- Chaotic, lost job, but now stable on Buprenorphine (Subutex) and has regained life
- Back pain persists so now unlikely to reduce further

#### Case 4 – anxiety and alcohol

- 53 year old married lady presented with alcohol dependency
- Primary anxiety disorder led to self medication with alcohol to combat social anxiety
- 2 detoxifications successful for approx 1 year abstinence maximum
- Engaged with all psychological and group recovery programmes available.
- Acamprosate and Naltrexone gave her significant side effects
- Successfully achieved ongoing abstinence with Baclofen 15mg o.d. with combined SNRI Duloxetine 50mg and CBT therapy

### Case 5 - GBL

- Academic with social anxiety who dabbled with Diazepam had been offered GBL liquid at night club
- Steady increase in use, purchasing this online anonymously
- Ran out of personal funds to continue
- Presenting hoping for outpatient detoxification
- Required transfer to IP input and required 200mg
   Diazepam to stabilize initially prior to detoxification.

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