Clozapine: What's It All About?

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Useful Resources

- Health Products Regulatory Authority (HPRA) available at hpra.ie.
- Link to medication patient information guides (HSE webpage):
  https://healthservice.hse.ie/staff/procedures-guidelines/medication-patient-information-guides-for-healthcare-workers/ - Link to HSE Choice and Medication website contained within section entitled: 'How to access the guides'
- Youth Med.info on clozapine, for children, teens and young adults: https://youthmed.info/medicines/clozapine/
- Clozapine: In Our Words – MHS consumer testimonials (10mins) https://www.youtube.com/watch?v=fIIE98Mv0rc
- Disclaimer – what we talk about today is the best available information today – may not be current tomorrow!

So What Is All The Fuss About?

Doesn't it kill people??

I wouldn't want to take it if it were me...

Isn't it just another antipsychotic?


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What is the prescription drug clozapine and is it dangerous?

Clozapine is said to be prescribed for around 37,000 Brits a year but can cause toxicity

Issues With Clozapine Use

- Clearly and unambiguously the gold standard agent for treatment-resistant schizophrenia
  - Works when other antipsychotics don’t
  - Efficacy builds over time
  - Keeps folks alive for longer and with a better QoL
  - Additional efficacy in suicidality and aggression
  - Doesn’t cause EPSEs including TD

- If we’re serious about recovery we need to use it as soon as someone meets criteria

Issues With Clozapine Use

- So why doesn’t it get used then??
  - Perceptions around adverse effects & retrials (C, P)
  - Perceptions around blood tests (C, P)
  - Perceptions around comorbidities e.g. cancer (C, P)
  - Perceptions around interactions e.g. cigarette smoke (C)
  - Perceptions around need for support at initiation e.g. inpatient admission, filling in forms (C, S)
  - Service fragmentation, lack of community support (S)

Issues With Clozapine Use

- And what does this reticence mean for patients?
  - Delay to effective treatment, increasing DUP
  - Poorer prognosis
  - More comorbidity
  - Increased risk of early mortality due to comorbidity or death by suicide/violence
  - Comparative inability to contribute to society or lead a fruitful life
  - Burden on family and carers

Issues With Clozapine Use

What are these “traffic lights” I hear about with clozapine??

Blood cell count		**Action required**	**Traffic light colour**
WBC/mm3 (/L)	**ANC/mm3 (/L)**	**-**	**-**
≥3500 (≥3.5 x 10^9)	≥2000 (≥2.0 x 10^9)	Continue clozapine treatment	GREEN
≥3000 to <3500 (≥3.0 x 10^9 to <3.5 x 10^9)	≥1500 to <2000 (≥1.5 x 10^9 to <2.0 x 10^9)	Continue clozapine treatment, sample blood twice weekly until counts stabilise or increase	AMBER
<3000 (<3.0 x 10^9)	< 1500 (<1.5 x 10^9)	Immediately stop clozapine treatment, sample blood daily until haematological abnormality is resolved, monitor for infection. Do not re-expose the patient	RED

Let’s Look at a Real Person - Diagnosis

- Danny is a 25 year old male
- Ongoing symptoms of psychosis despite two months of olanzapine at 20mg/day (adherence confirmed) and six months of paliperidone LAI 150mg. Currently back on olanzapine 20mg/day.
- No physical health issues, no substance use.

Let’s Look at a Real Person - Swapping

- Generally use a cross-titration to minimise risk of mental state deterioration, but promptly to minimise additional risk of blood dyscrasias

- Principles-based – monitor closely and be prepared to flex!
  - Think about half lives
  - Pharmacology of both agents – which neurotransmitter systems?
  - Initiation titration/effects v additive effects v withdrawal effects
  - Dosing (timing/splits) and forms
  - Reason, setting and complexity will dictate speed
  - Think abut what monitoring is needed and when to escalate

Let’s Look at a Real Person - Levels

- Three clozapine levels were performed at fortnightly intervals on a dose of 100mg mane and 250mg nocte at steady state and were:
  - 0.45mg/L (with norclozapine 0.31mg/L)
  - 0.61mg/L (with norclozapine 0.32mg/L)
  - 0.4mg/L (with norclozapine 0.29mg/L)
  - The usual range 0.35-0.50mg/L, with norclozapine usually around 70% of clozapine levels)
- How would you interpret these?

Let's Look at a Real Person – Adverse Events

- What would you do if Danny told you he was experiencing:
  - Drowsiness?
  - Drooling?
  - Constipation? – or diarrhoea? DO NOT TAKE THIS LIGHTLY!
  - Dizziness?
  - Sore throat/flu-like symptoms/generally unwell?
  - Wetting the bed at night?
  - Weird jerky muscle twitches?
  - Breathlessness?

  - Or told you he wanted to stop or was restarting smoking?

  - Or told you he hasn't been taking his clozapine recently?

Let’s Look at a Real Person – Counselling

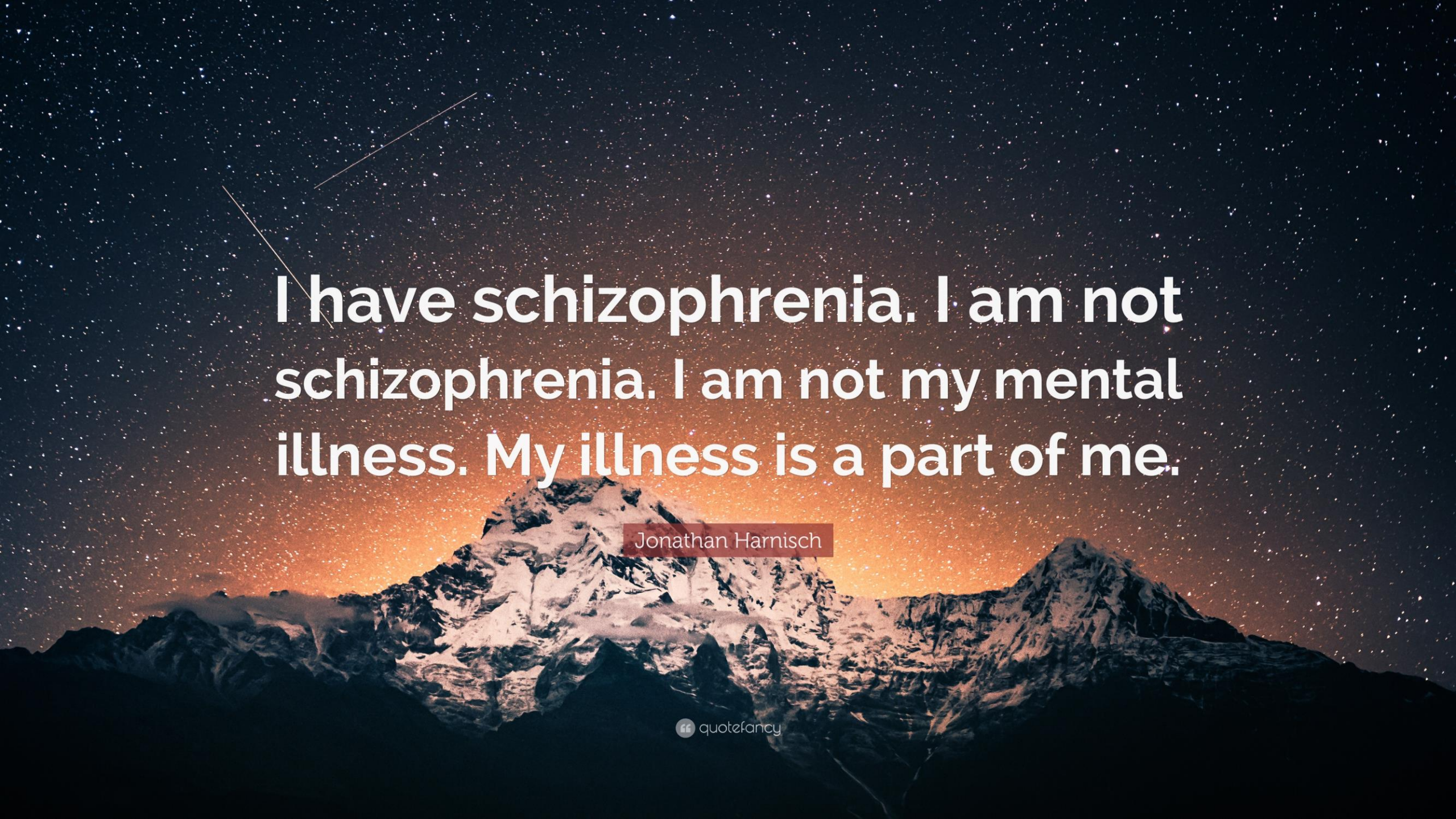
- Stay on the clozapine!
- Tell all HPs you take it – GP, community pharmacist, dentist, if you go to hospital
- Deal with signs/symptoms of infection, and constipation
- Tell your team if you start/change/stop smoking
- How to manage alcohol and clozapine sensibly
- Systems and processes for supply and monitoring
- Plan your holidays with your team – in advance!

Let’s Look at a Real Person – Circumstances

- But they can’t take it?
- But they won’t take it?
- But it’s not working?

Let’s Look at a Real Person – Making It Work

- Communication at interfaces with relevant people is key, as is medicines reconciliation – GPs, community pharmacy, CMHTs, inpatient MHS, inpatient acute
- Ensure clozapine is entered onto relevant patient records systems as a heads up, especially for folks that don’t prescribe or dispense it
- Sense check family/carer involvement if he wants that


I have schizophrenia. I am not schizophrenia. I am not my mental illness. My illness is a part of me.
Jonathan Harnisch
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