

BMC Youth Model Seminar #8

Circadian-based Mood Disorders: Bipolar and Atypical Depression

Assessment and Intervention

Presented by

A/Professor Elizabeth Scott

e.scott@sydney.edu.au



Acknowledgements

- Of country
- Of lived experience

Overview

1. Assessment and routine outcome monitoring
2. Evidence-based and personalised care
 - Non-pharmacological interventions
 - Pharmacological interventions
3. Case example

Personalising treatment plans and monitoring outcomes

OPINION

Open Access

Manipulating the sleep-wake cycle and circadian rhythms to improve clinical management of major depression

Ian B Hickie^{1*}, Sharon L Naismith¹, Rébecca Robillard¹, Elizabeth M Scott^{1,2} and Daniel F Hermens¹

Abstract

Background: Clinical psychiatry has always been limited by the lack of objective tests to substantiate diagnoses and a lack of specific treatments that target underlying pathophysiology. One area in which these twin failures has been most frustrating is major depression. Due to very considerable progress in the basic and clinical neurosciences of sleep-wake cycles and underlying circadian systems this situation is now rapidly changing.

Discussion: The development of specific behavioral or pharmacological strategies that target these basic regulatory systems is driving renewed clinical interest. Here, we explore the extent to which objective tests of sleep-wake cycles and circadian function - namely, those that measure timing or synchrony of circadian-dependent physiology as well as daytime activity and nighttime sleep patterns - can be used to identify a sub-class of patients with major depression who have disturbed circadian profiles.

Developing an evidence-base for selection of sequences of care:

1. Psychological/behavioural; 2. Pharmacological; 3. experimental

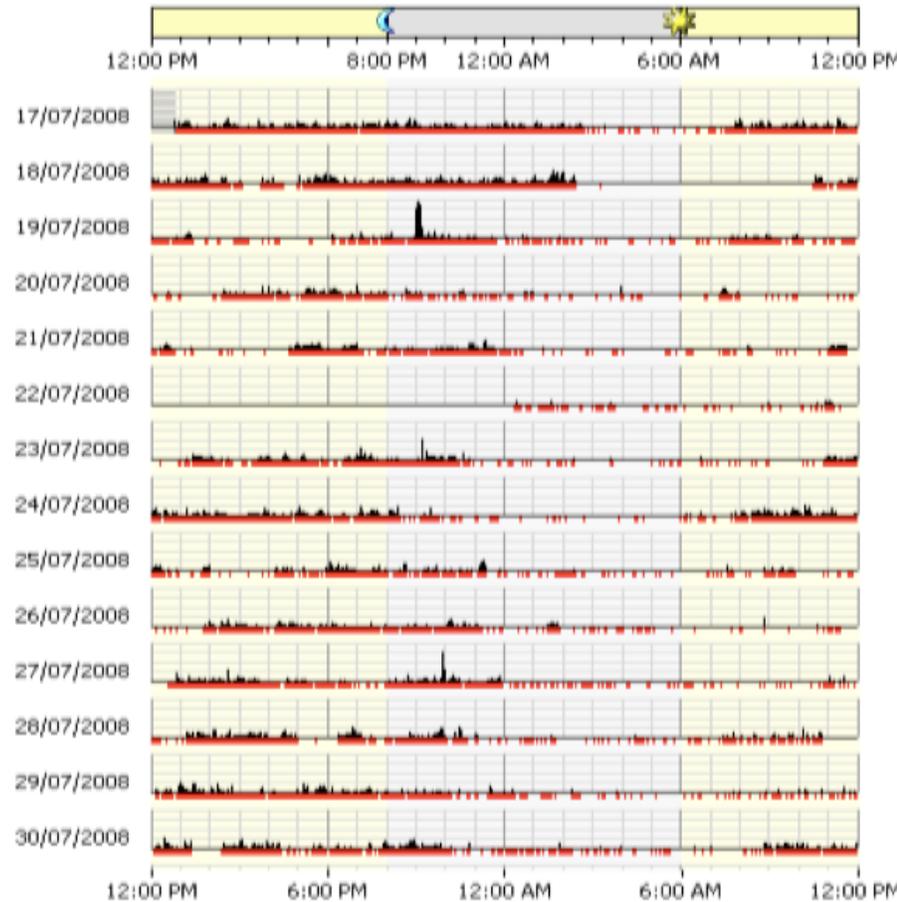
Depression Type	Psychological / Behavioural	Pharmacological	Experimental
1. Anxious-Depression	CBT, IPT, Problem-Solving	SSRIs, SNRIs	DCS
2. Circadian-Fatigue / Depression	Behavioural, Physical Activity Sleep-Wake Cycle Circadian-CBT Sleep Deprivation Therapy Actigraphy and DLMO assay	Melatonin Melatonin analogues Lithium Anticonvulsants	Fish Oils Stimulants Modafinil TMS/DBS Ketamine
3. Developmental / Psychosis	Social Skills Training Cognitive Remediation Educational	Stimulants Anticonvulsants Fish Oils	Novel Neuropeptides Glutamate Regulation Dopamine Regulation

Actigraphy Recordings in Humans



- Patterns of physical activity over 24 hour periods
- Two weeks of recording – differentiate weekends/weekdays
- Variability in daily patterns
- Sequencing of relationships to mood, cognition, physical health outcomes
- Optimizing analytical systems
- Relationships to body temp, light exposure

Selected young patient with bipolar disorder (depressed)



- Late Rising
- Poor Regularity
- Disturbed Sleep
- Lower total activity than expected
- (seasonal onset of hypomania/mania)

Optimising your 24hr body clock to improve your sense of wellbeing



Creating a synchronised 24hr body clock:

Morning and afternoon activity



- › Get out and exercise in the morning sunlight
 - ❖ Suppresses melatonin earlier
 - ❖ Increases your core body temperature and heart rate
- › Take an afternoon walk
 - ❖ Get past the 3pm low
- › Be active rather than sedentary
 - ❖ Improves your metabolism, eating, and weight

Creating a synchronised 24hr body clock:

Morning light

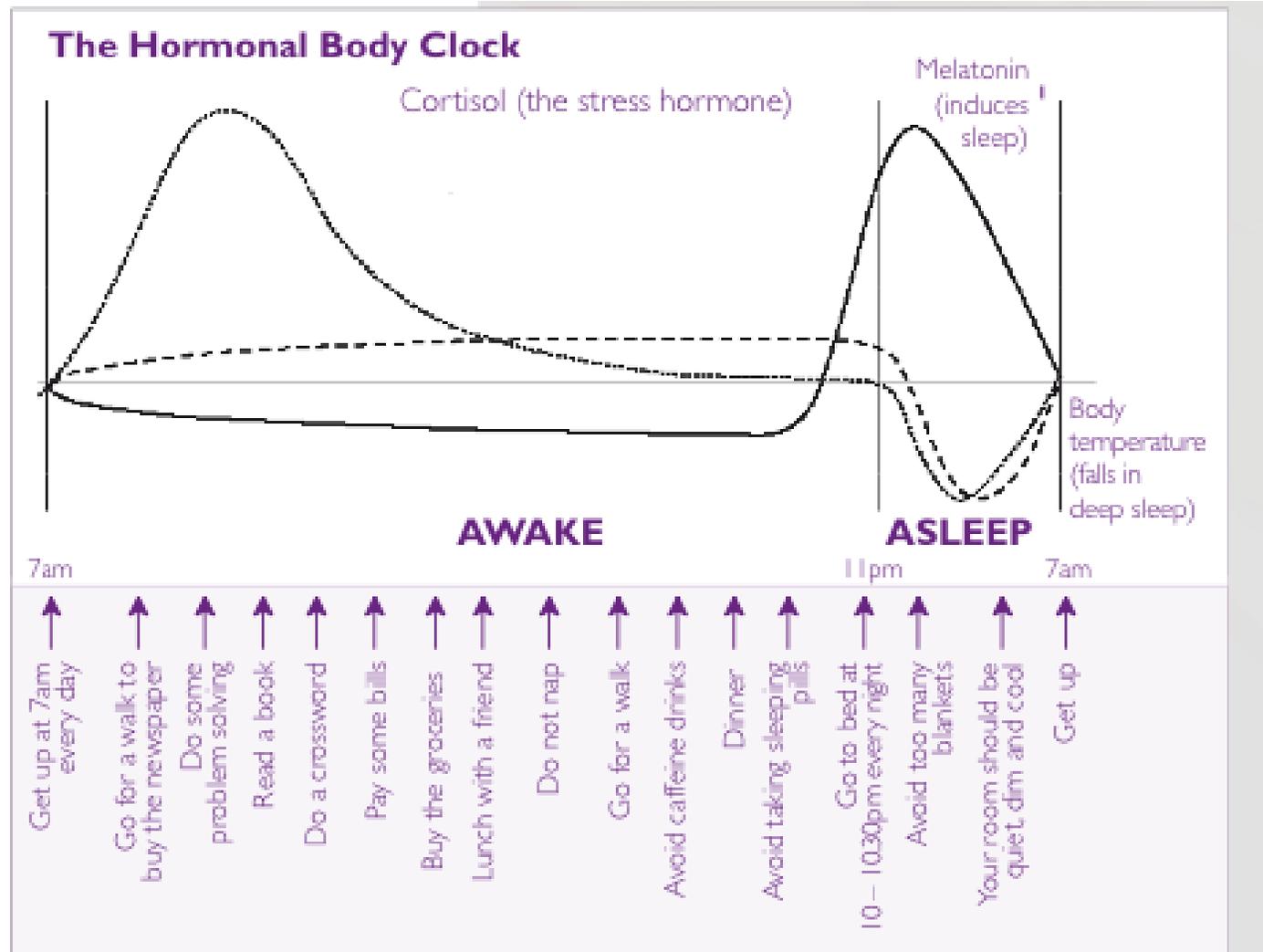
- **Get morning light**
 - ❖ Suppresses melatonin
 - ❖ Increased body temperature
- **Morning light can shift your bedtimes forward**
 - ❖ As melatonin is suppressed earlier
- **Shake you out of that zombie-like state**
 - ❖ Feel more awake and energetic for the day ahead



BMC Guide to Depression Management: Restoring Your Sleep-wake (Circadian) Cycle



Sleep cycle interventions



Source: SPHERE 'A Depression Management Program Incorporating Cognitive Behavioural Therapy Strategies' 2000.

Activity Scheduling (IPSRT/Circadian therapy)

1. Sleep hygiene and regular sleep onset and offset
2. Regular meal times
3. Regular and early social rhythms
 - Social exercise and/or Social interaction
4. Minimise over stimulation
 - Pace activity
 - Avoid late nights, multiple events, social overload
5. Use behavioural activation to address under stimulation
 - Plan and engage in activities that are pleasurable and/or give a sense of achievement or mastery
 - Set small goals with stepwise progression
6. Identify interpersonal sources of support or disruption
7. Take medication at regular times
8. Track activity and progress

Mood diary

Daily mood rating	1	2	3	4	5	6	7
	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
10 (elevated mood or irritable mood)							
9							
8							
7							
6							
5 (normal mood)							
4							
3							
2				x			
1		x	x		x		
0 (worst depressed mood)	x					x	x
Hours of Sleep (night)	4	5	4	4.5	5	3	4
Other comments	Bad day. No energy. Stayed in bed.	Bad morning. Got up at midday. Felt a bit better.	Felt sick. Nauseous and tired. Tried to do some study.	My sister came over and got me out of bed. Felt better in the evening.	Bad morning, got up and had a shower, went back to bed.	Mum called and tried to get me to go out with her. Had to go home.	Agitated and anxious, worried about my course.

What was your best day this week? Thursday

What was your worst day this week? Monday

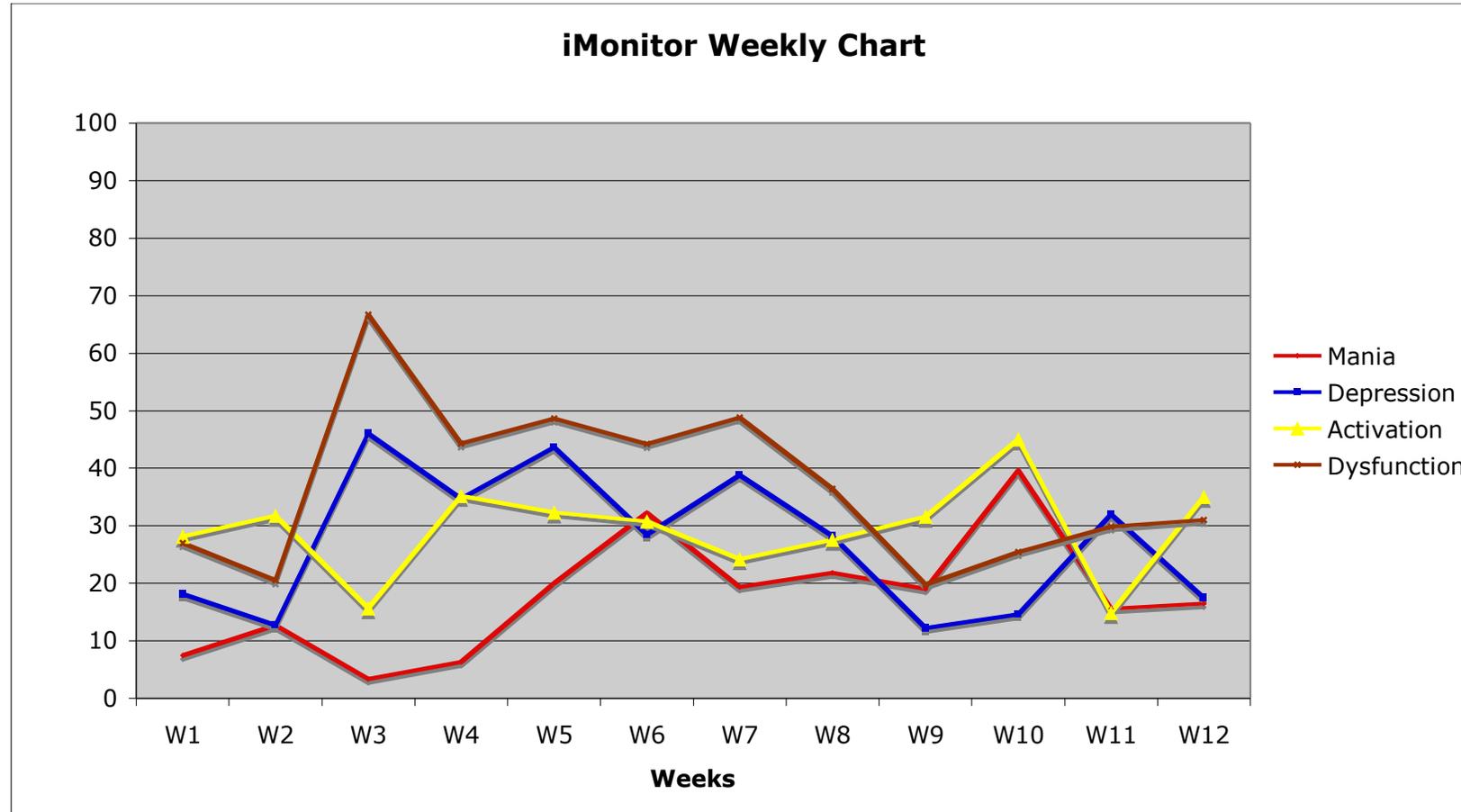
What were you doing? Spent the day with my sister.

What were you doing? Stayed in bed.

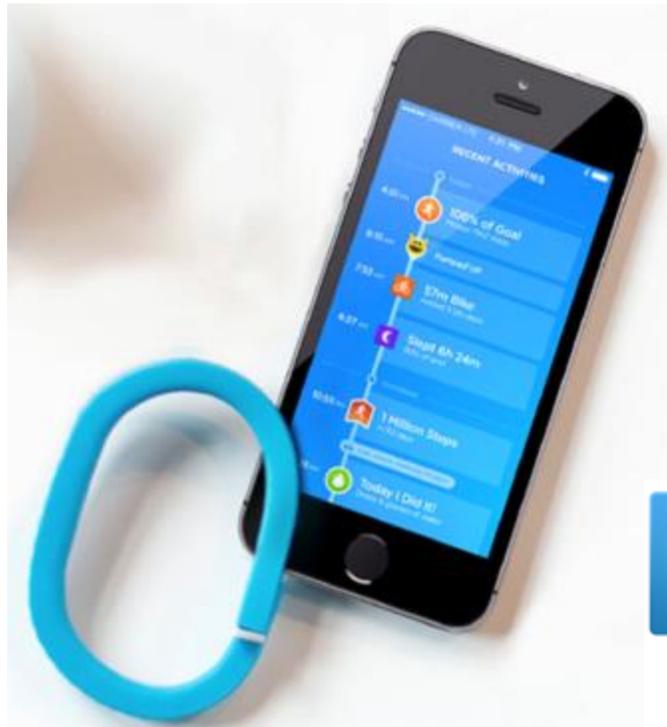
What were you thinking? I am feeling better. I can do this!

What were you thinking? I can't cope. I'm going to fail my course.

Monitoring of daily symptoms



Monitoring technologies and sleep-activity apps



Wello



Sleepio



Lose It!



FitCoin



Tictrac



GymPact



RunKeeper



MyFitnessPal



MapMyFitness



FitStar



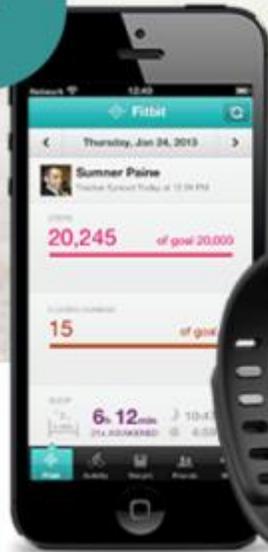
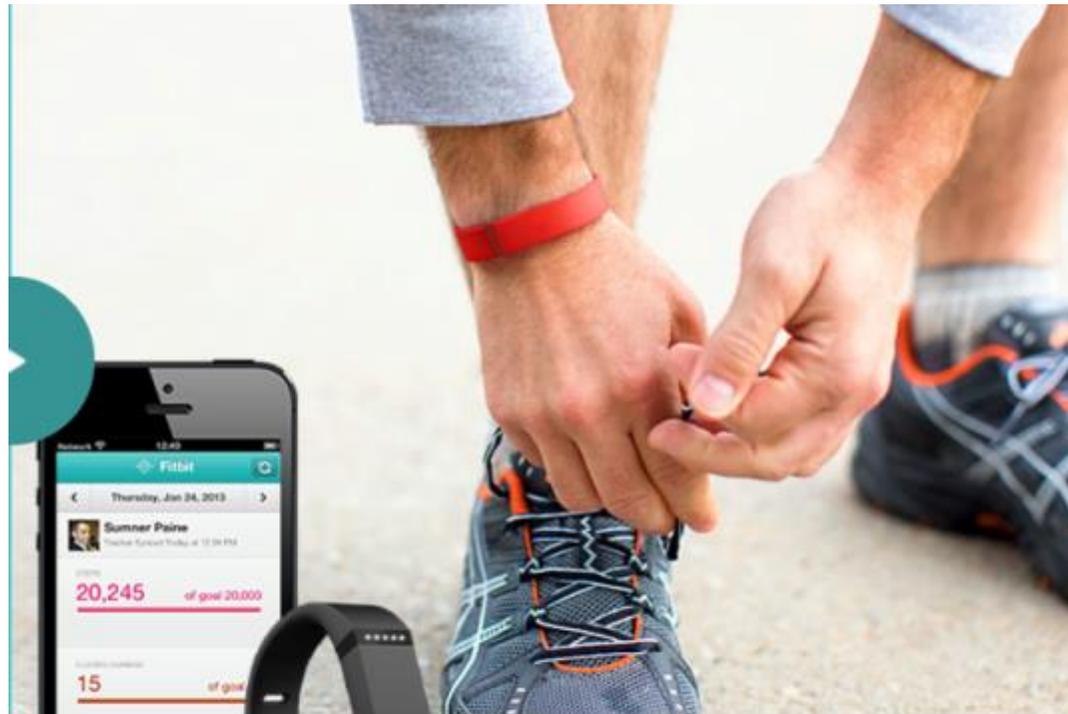
IFTTT



Strava



Regular activity (in daylight) – every day! (24 hour cycles matter....)



Flex™ Wireless Activity & Sleep Wristband

BUY NOW A\$129⁹⁵



Personalised and measurement-based care

Personalised

The notion that the assessment of, and the sequence of interventions and services are tailored to the individual, and their needs.

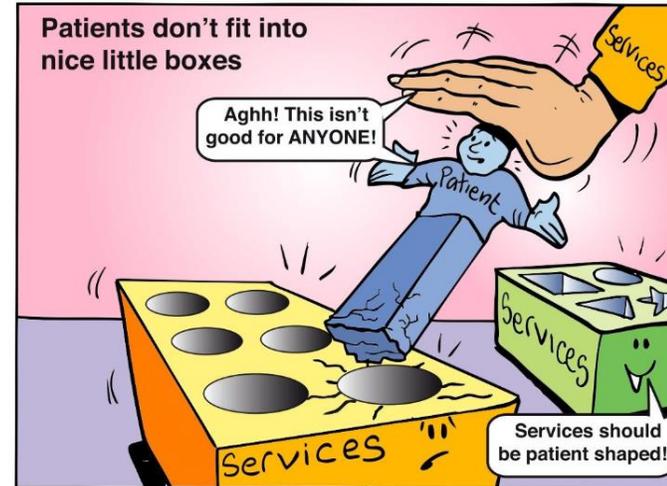


Measurement-based

The use of systematic and continued assessment of outcomes to guide clinical decision-making (i.e. data driven approach)

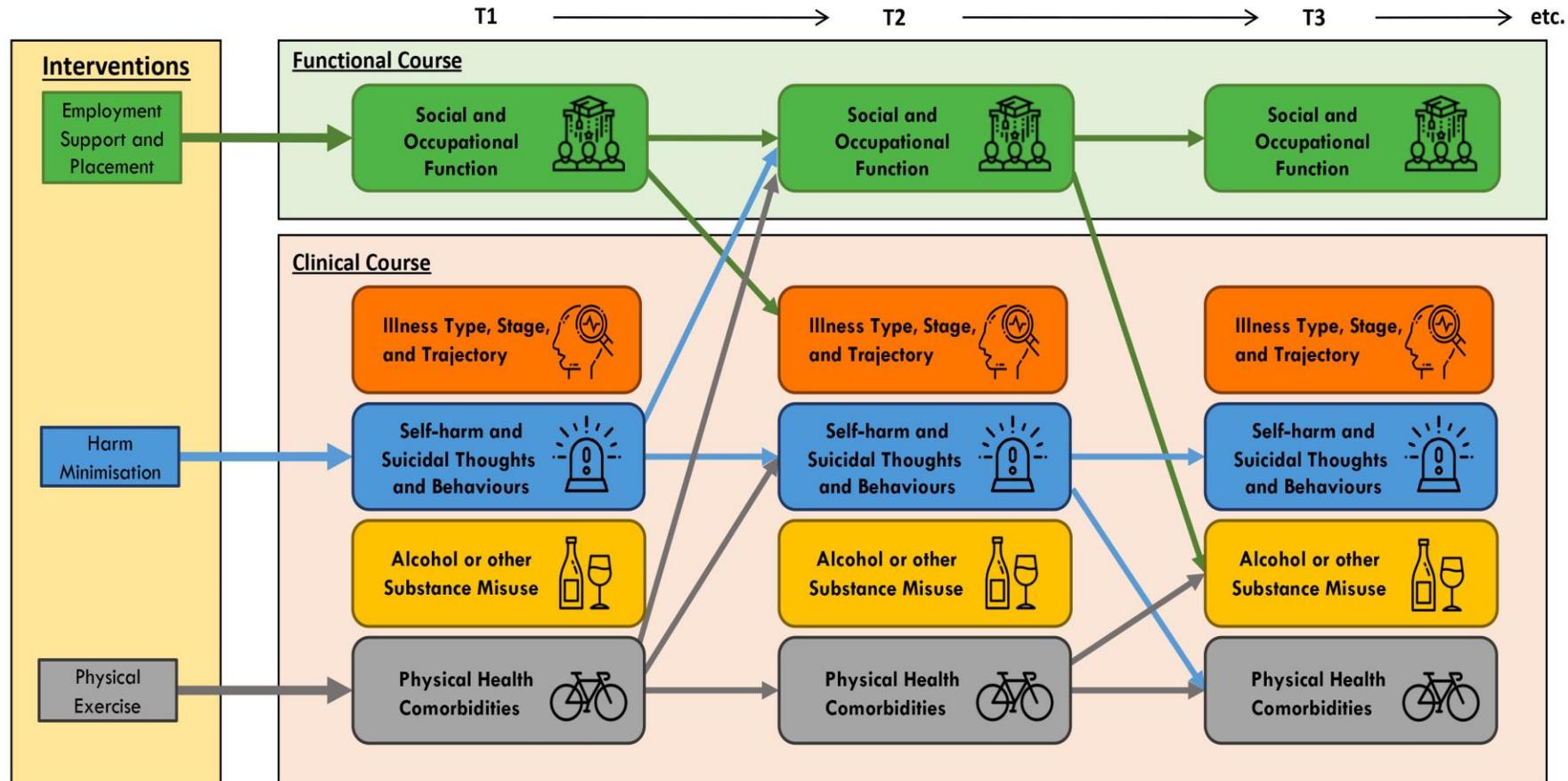


Right care, right time!



Cascading impacts of interventions on outcomes

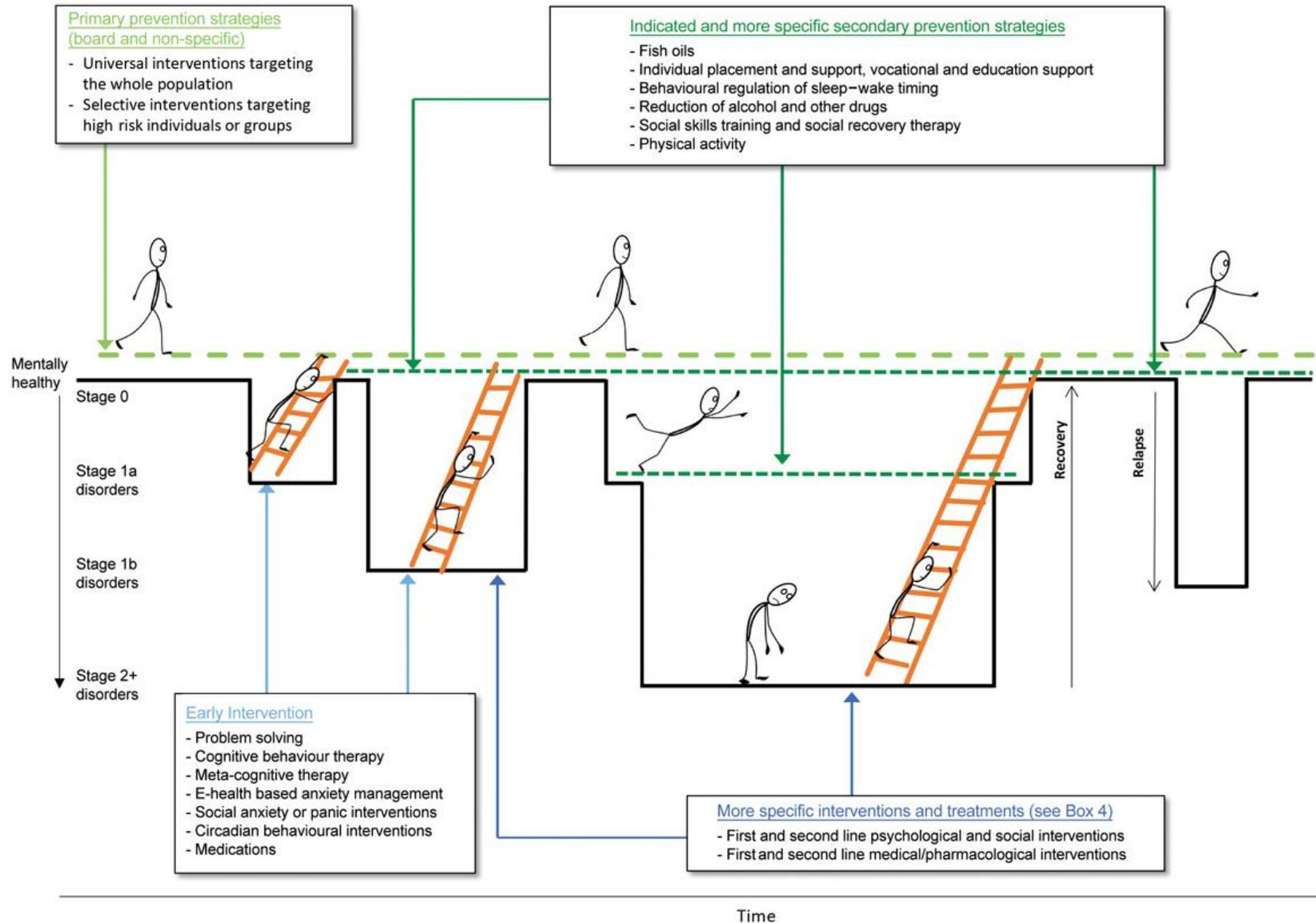
A multidimensional approach helps to unravel the complex relationship between these different outcomes, and plan appropriate interventions



Interventions which target individual domains are likely to have specific and **direct impacts**, as well as **indirect impacts on other domains**, which cascade over time.

Trajectory of mental disorders and sequence of interventions

Rohleder et al., 2019 - MJA



Illustrative example of personalised and measurement-based care in practice, using technology

Legend



Clinical contacts with the health service



The use of the Platform to track a young person's progress
Green=improvement, red=deterioration, =notification



The use of the Platform in shared-decision making

2. Initial assessment

The Platform notifies the health professional that a young person has a higher need for care. Instead of waiting the usual amount of time, an earlier first appointment is organized.

1. Presents for care

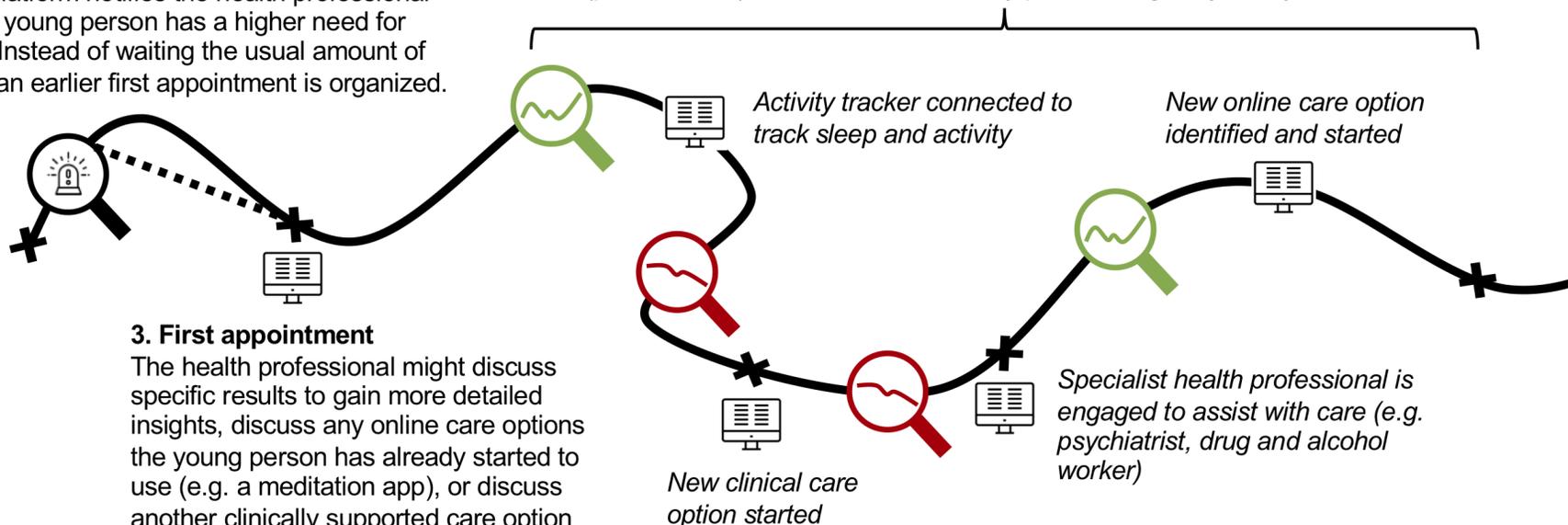
A young person who presents to a health service is sent an invitation email to access the Platform

3. First appointment

The health professional might discuss specific results to gain more detailed insights, discuss any online care options the young person has already started to use (e.g. a meditation app), or discuss another clinically supported care option which might be available or useful (e.g. group therapy for anxiety).

4. Ongoing measurement-based care

The Platform facilitates ongoing data collection over the course of the active care period to track the course of illness and multidimensional outcomes so the young person and their health professional can make real-time, new (personalized) clinical decisions at key points along the journey.



Where are we at with assessment and treatment options?

Circadian therapy aimed at: Shorter period, phase advance, stable rhythms

- **Assessment**
 - Multi-modal, ACTIGRAPHY, Metabolic/Hormonal/Inflammatory-Immune screen
- **CBT- based options**
 - BEHAVIOURAL REGULATION. MORNING LIGHT EXPOSURE. PHYSICAL ACTIVITY/EXERCISE
 - ICBT-insomnia
 - Mindfulness based CBT
- **Melatonin and analogues**
 - Impact on SLEEP and DEPRESSIVE SYMPTOMS
- **Orexin Antagonists**
- **Rhythm Stabilization**
 - BRIGHT LIGHT THERAPY/LITHIUM
- **Sequencing of treatments**

Psychological and pharmacological treatment options

Psychological and behavioural therapy aimed at:

- › maintaining stable sleep, regular exercise and activity patterns
- › reducing and managing anxiety and stress
- › reducing rumination, improving self esteem, emotional regulation skills
- › minimising substance use
- › improving impulse control
- › return to work and study

Pharmacological therapy aimed at:

- › Improving and stabilising mood – antidepressants/mood stabilisers
- › preventing relapse
- › minimising metabolic disturbance – lamotrigine/aripiprazole

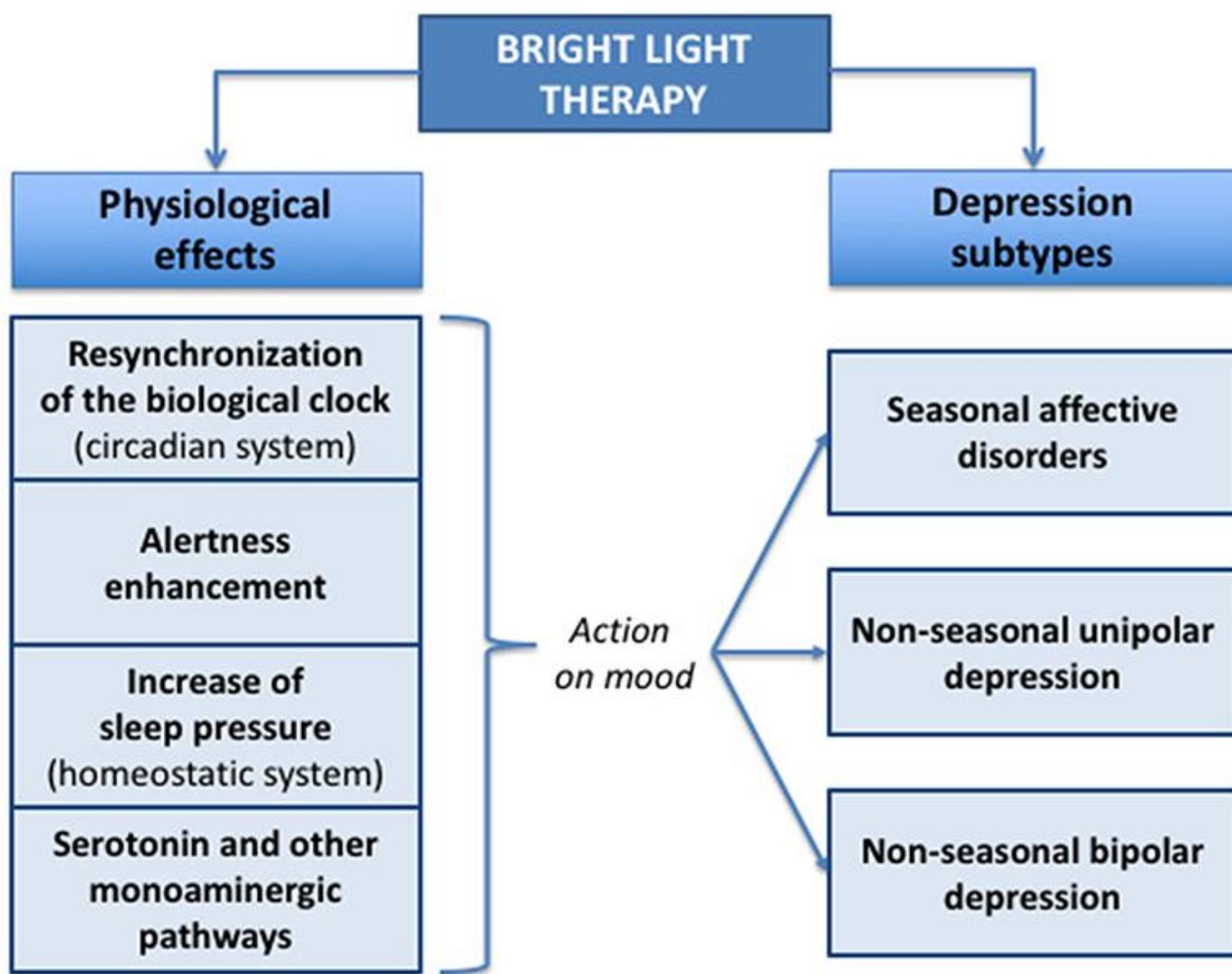
Scheduling therapy

Ultra high-risk or early symptoms	<ul style="list-style-type: none">›Circadian rhythm/sleep wake cycle therapy›CBT/DBT emotional regulation skills›Medication (melatonin, omega 3 fatty acids)
Early illness	<ul style="list-style-type: none">›Medication (agomelatine, SNRI, MAOI's, bupropion, lamotrigine, modafanil)›Circadian rhythm/sleep wake cycle therapy›CBT/DBT emotional regulation skills›Self monitoring›Vocational/education support›Family/carer psychoeducation and support
Established illness	<ul style="list-style-type: none">›Medication (mood stabilisers)›IPSRT/circadian therapy›CBT for some patients›Self monitoring›Cognitive remediation›Vocational/education support

Bright Light Therapy

	Seasonal affective disorder (SAD)	Non-seasonal unipolar disorder	Non-seasonal bipolar disorder
Light intensity	2,500–10,000 Lux Or low-intensity blue-enriched light	2,500–10,000 Lux	<10,000 Lux
Dose (Exposure durations/Intensity of illumination)	First line: 10,000 Lux for 30 min/day Also consider: 5,000 Lux for 1 h/day or 2,500 Lux for 2 h/day		Slower increase For instance: 5,000 Lux with increase of 15 min per week until 60 min at one month (depending on efficacy and tolerance)
Lamp disposition		lamp at eye level distance of 30–80 cm (depending on the device recommendations)	
Frequency Administration	Daily Mono- or adjunct-therapy		Daily Only with a mood stabilizer with antimanic properties
Time of the day	Early morning (for instance: 8 am, chronotype may be considered)		Midday (especially if there is an history of manic switch) Or Early morning
Onset of response		1 week	
Duration of treatment	Until the period of usual spontaneous remission in the spring or summer	2–5 weeks	Until reduction of depressive symptoms or maintained in case of relapse when stopped
Prevention	Possibility to treat by light therapy a few weeks before the usual seasonal depressive relapse period	NA	NA
Adverse effects	Manic switch and mild side effects (headache, eyestrain, nausea, and agitation)	Mild side effects (headache, eyestrain, nausea, diarrhea, and agitation)	Manic switch and mild side effects (headache, eyestrain, nausea, and agitation)
Contraindications	Ophthalmic disorders (cataract, macular degeneration, glaucoma, retinitis pigmentosa), and disorders affecting the retina (retinopathy, diabetes, herpes, etc.)		

NA, data not available.



Stabilising circadian rhythms and depression – Pharmacological Agents

- Melatonin - sleep onset/offset, stability (not an antidepressant/no antidepressant activity)^{1,2}
- Agomelatine: agonist MT₁/MT₂ and antagonist 5-HT_{2C}³
 - Helps resynchronise circadian rhythms in patients with depression^{1,3,4-9}
- Lithium – lengthen period, inter-episode effects
- Stimulants and other vigilance agents - modafanil
- Roles of other antidepressants – positive or negative
- Other Mood Stabilizers – lamotrigine

1. Hickie IB & Roger NL *The Lancet* 2011;378:621-31 2. Srinivasan V et al *World J Biol. Psychiatry* 2006;7:138-151 3. Valdoxan Approved Product Information 4. Leproult R et al *Clin Endocrinol.* 2005;63:298-304 5. Kasper S et al *Clin Psych.* 2010;71(2):109-120 6. Lemoine P et al *J Clin Psych.* 2007;68:1723-1732 7. Redman J et al *J Biol. Rhythm* 1998;13:39-51 8. Armstrong S et al *Pharm Biochemistry & Behav* 1993;46:45-49 9. Boivin DJ et al *Psych Neurosci.* 2000;25:446-58

Developing an evidence-base for selection of sequences of care:

1. Psychological/behavioural; 2. Pharmacological; 3. experimental

Depression Type	Psychological / Behavioural	Pharmacological	Experimental
	CBT, IPT, Problem-Solving	SSRIs, SNRIs	DCS
2. Circadian-Fatigue / Depression	Behavioural, Physical Activity Sleep-Wake Cycle Circadian-CBT Sleep Deprivation Therapy	Melatonin Melatonin analogues Lithium Anticonvulsants	Fish Oils Stimulants Modafinil TMS/DBS Ketamine
3. Developmental / Psychosis	Social Skills Training Cognitive Remediation Educational	Stimulants Anticonvulsants Fish Oils	Novel Neuropeptides Glutamate Regulation Dopamine Regulation

Case example – assessment and experience of care



Case Example – Assessment and Treatment Planning

- Mood and anxiety sx – *CBT/DBT, optimize antidepressant, ?mood stabiliser*
- Sleep/activity patterns – *behavioural activation/exercise/light therapy*
- Physical health assessment – *investigations and interventions*
- Metabolic screening – *tx of insulin resistance (diet, exercise, metformin)*
- Hormonal screening and assessment – *tx of PCOS*
- Drug and alcohol assessment – *reduce alcohol*
- Neurocognitive assessment – *educational support*
- Social communication skills/social network – *CBT/IPSRT*
- Family assessment – *psychoeducation and intervention*

Summary...

- Can the course of circadian/bipolar-type illness be modified?
 - Environmental interventions (circadian-based behaviour therapies)
 - Pharmacologic (melatonin, melatonin analogues, lithium)
- Interventions to *re-set, resynchronize or stabilize* (i.e. make less sensitive to repeated disruption) these circadian-based phenomena



Thank you!

*CPD points can be claimed for psychologists, psychiatrists, social workers, occupational therapists, and mental health nurses.
Please contact grace.lee@sydney.edu.au for more information.*

The Brain and Mind Centre would like to thank our research partners, such as



END