The role of the general practitioner in managing the physical health as well as the mental health of patients on antipsychotics

Matthew Warden
Director AIS, St Vincent's Hospital Melbourne

Targeting zero: Implications for Australian Mental Health Service (Newton et al, 2017)

"If we are able to reduce the gap in psychiatric morbidity and mortality and support people in leading a life worth living and filled with hope and power within the community, then psychiatrists have a responsibility to provide them with the best treatment possible and be strong and consistent advocates for the resources to provide treatment and services they need".

Study of High Impact Psychosis: SHIP (2010)

- **7 catchments across 5 States covering 1,319,519 people**
- **Total number interviewed (Apr–Dec 2010): 1,825 (screen positive) + 164 (screen negative)**

Two phase design:
Phase 1:

- Census month March 2010: those in contact with services were screened for psychosis
- 11 months prior to census: all administrative records were scanned for psychosis

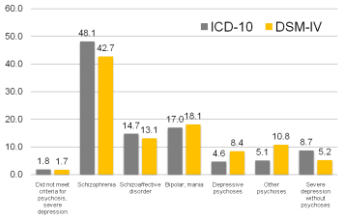
Phase 2:

- Randomised stratified sampling by age group (18–34, 35–64)

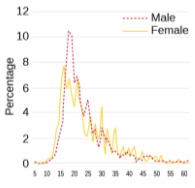
Morgan et al. ICOSR 2011

Findings: Mental Health

Diagnostic profile %



Age at onset %



Morgan et al. ICOSR 2011

Physical activity by sex and age

	Men (N=1083)	Women (N=736)	18–34 years (N=768)	35–64 years (N=1051)	Total (N=1819)
Very Low	**32%**	**35%**	29%	37%	**34%**
Low	**64%**	**62%**	67%	61%	**63%**
Moderate	**3%**	**2%**	4%	2%	**3%**
High	**0.3%**	**0.2%**	0.2%	0.3%	**0.3%**

BMI by age and sex

	Men (N=1067)	Women (N=707)	18–34 years (N=753)	35–64 years (N=1021)	Total (N=1774)
Underweight BMI < 18.5	**1%**	**2%**	3%	0.004%	**1.5%**
Normal BMI = 18.50 – 24.99	**23%**	**23%**	29%	19%	**23%**
Overweight BMI 25.00 – 29.99	**33%**	**23%**	30%	29%	**29%**
Obese > 30	**42%**	**53%**	39%	52%	**46%**

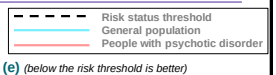
Diabetes/hyperglycaemia, bp, lipids by age & sex: undertreatment

	Men N (%)	Women N (%)	Total N (%)	Taking medication for this condition (N)	Percentage of those diagnosed with the condition taking the medication to treat it
Diabetes or hyperglycaemia	20%	22%	21%	149	40%
Hypertension	19%	21%	20%	182	52%
High cholesterol	29%	34%	31%	211	39%

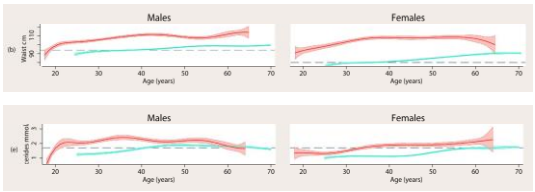
Metabolic risk factors and treatment – fasting bloods (n=1286)

	Normal, not treated	Normal on medication for this condition	At-risk, not on medication for this condition	At-risk, on medication for this condition	Total at-risk
Glucose	69.0%	2.3%	22.7%	5.9%	28.6%
HDL-C	45.2%	5.0%	42.6%	7.0%	49.6%
Triglycerides	48.6%	3.3%	39.4%	8.6%	48.0%
Hypertension	46.6%	3.9%	42.1%	6.5%	47.5%

Cardiometabolic profile by age and sex

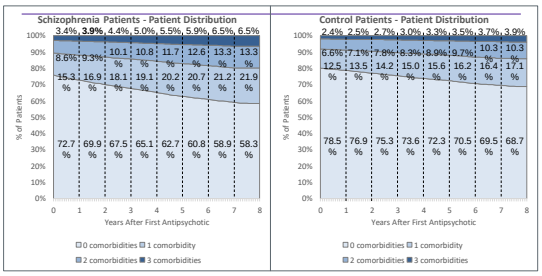


Waist circumference (b) and triglycerides (e) *(below the risk threshold is better)*



from Foley D *et al.* Cardiometabolic risk indicators that distinguish adults with psychosis from the general population PLoSONE. 2013, 8, e82606

Distribution of the number of treated comorbidities per patient following initiation of treatment for schizophrenia compared to matched controls



The percentage distribution of schizophrenia patients based on the number of comorbidities the have following initiation of treatment for schizophrenia. Maximum comorbidities is 3: Diabetes, Hyperlipidemia, Hypertension.

The percentage distribution of age and gender matched control patients based on the number of comorbidities for comparison against treated schizophrenia patients

Targeting zero: Implications for Australian Mental Health Service (Newton et al, 2017)

"RANZCP guidelines are helpful at collating much of the evidence and identifying elements of good care, but have not set a clear standard of care content that we can be held accountable to".

Clinical practice guideline for the management of schizophrenia and related disorders

Professor Cherrie Gallety (Chair)

Professor David Castle

Nga Tran

---- on behalf of the writing group

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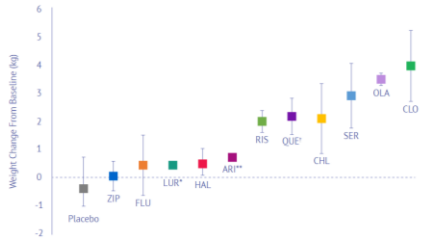
Table 3: Physical assessment and investigations for people presenting with first-episode psychosis

Physical examination including neurological examination
Full blood count and ESR
Electrolytes, liver function tests
Fasting glucose, cholesterol, triglycerides
Thyroid function tests
Hepatitis screen (with tests for other blood-borne diseases e.g. HIV if indicated)
Anti-NMDAR, Anti-VGKC, Anti-GAD antibodies§
Urine drug screening
ECG
EEG (if indicated)
MRI scan of the brain (if indicated)
Psychometric testing (if possible)
Screening for sexually transmitted diseases (if indicated, including HIV)

Recommendations on medication in first-episode psychosis	Type	Level of evidence
The management plan should be discussed fully with the individual and their family/carers, wherever possible. The benefits and risks of drug therapy should be explained in a non-coercive manner.	EBR	II
Medication should be used in combination with psychosocial interventions, including strategies to encourage adherence to medicines.	EBR	II
The choice of antipsychotic medicines should be based on: • the individual's preference after risks and potential benefits have been explained • the person's prior response to the medicine (if known) • clinical response to an adequate treatment trial • individual tolerability • potential long-term adverse effects.	EBR	I
The lowest effective antipsychotic dose should be used to establish treatment acceptance and minimise side effects.	EBR	II
Prescribe only one antipsychotic agent at a time, unless it has been clearly demonstrated that the person's symptoms are resistant to monotherapy.	EBR	II
Prescribe antipsychotic medicines at doses that are adequate to prevent relapse, suppress symptoms and optimise the person's subjective wellbeing.	EBR	II
Provide an adequate duration of treatment. Monitor treatment and adverse effects appropriately.	EBR	II
Consider the use of long-acting injectable antipsychotic medicines if: • the individual prefers a long-acting injectable medicine • adherence has been poor or uncertain • there has been a poor response to oral medication.	EBR	II
Treatment with clozapine should be considered early if appropriate pharmacological interventions are ineffective.	EBR	I

Mean change in weight after 10 weeks of antipsychotic treatment

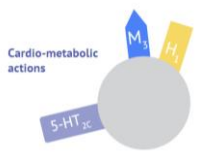


ZIP: Ziprasidone; FLU: Fluphenazine; LUR: Lurasidone; HAL: Haloperidol; ARI: Aripiprazole; RIS: Risperidone; QUE: Quetiapine; CHL: Chlorpromazine; SER: Sertindole; OLA: Olanzapine; CLO: Clozapine.

*Data pooled from short-term, placebo-controlled studies[2]; **4-6 week pooled data[3];†6-week data.

1. Allison DB, et al. *Am J Psychiatry*. 1999;156(11):1686-1696. 2. LATUDA® (lurasidone HCl) Approved Product Information. 3. Marder SR, et al. *Schizophr Res*. 2003;61(2-3):123-136.

Potential for antipsychotic-induced metabolic adverse effects



High metabolic risk: clozapine, olanzapine[1]

Moderate metabolic risk: risperidone, paliperidone, quetiapine[1]

Low metabolic risk: ziprasidone, aripiprazole, lurasidone, asenapine[1]

- Other unknown receptors or factors may also contribute to the development of metabolic syndrome.
- The correlation between receptor binding affinities and clinical outcomes is uncertain.

1. Stahl SM. *Stahl's Essential Psychopharmacology*. 4th ed. 2013.

Relative frequency of atypical antipsychotic-induced metabolic and cardiovascular adverse effects

Antipsychotic agent	Weight gain	Hyperglycemia	Dyslipidemia	Orthostatic hypotension	QTc prolongation
Amisulpride	+	-	?	-	++
Aripiprazole	-/+	-	-	+	-
Asenapine	+	++	++	+	+
Clozapine	+++	+++	+++	+++[b]	+
Lurasidone	+/-	+/-	-	-	-
Olanzapine	+++	+++	+++	+	+
Paliperidone	++	+	++	++[b]	+
Quetiapine	++	+++	++	++	++
Risperidone	++	++	++	++[b]	+
Ziprasidone	+	+	-	+	++

Adapted from Galletly et al 2016.

?: Little to no information; -: Negligible or absent; +: Infrequent; ++: Moderately frequent; +++: Frequent.

[a]Weight loss reported;[b]Reported to occur but no definitive data published as to the incidence;[c]Frequency may be higher at the start of therapy or with rapid dose increase;[d]Frequency may be higher with rapid dose increase, but data are conflicting;[e]More frequent with rapid dose increase.

1. Galletly C, et al. *Aust N Z J Psychiatry*. 2016;50(5):410-472.

Key consideration

Regular screening and intervention for cardiometabolic problems in people with schizophrenia should be mandatory, from the first episode of psychosis

Table 7. Monitoring for people taking antipsychotic medication

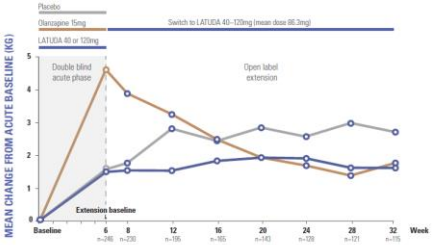
	Baseline	4 weeks	8 weeks	12 weeks	24 weeks	Annually
Patient history	X					X
Weight (BMI)	X	X	X	X	X	X
Waist circumference	X			X	X	X
Fasting plasma glucose, HbA1c	X			X	X	X
Fasting lipid profile	X			X	X	X
Prolactin	X	$	$	$	X	X
Full blood count	X				X	X
ECG	X				X	X
EEG	X					
Pregnancy test	X	$	$	$	$	$
Ophthalmological examination	X%					X%

Recommendations relating to physical health of people with psychosis	Type	Level of evidence
Engage the individual and carers in strategies to ensure healthy living (e.g. diet, exercise).	EBR	III-1
If the person is gaining weight or has other metabolic complications of treatment, switch to a weight-neutral antipsychotic agent.	EBR	II
Consider the use of agents such as metformin to reduce weight gain and insulin sensitivity in people taking antipsychotic agents associated with obesity.	EBR	II
Liaise with the GP to ensure optimal treatment for hypertension, elevated cholesterol and other cardiometabolic conditions.	CBR	N/A
For people who do not attend a GP, consider undertaking investigations, monitoring and prescribing as needed to treat physical health problems within the mental health service.	CBR	N/A
Liaise with an endocrinology specialist or other specialist colleagues as appropriate.	EBR	IV
All mental health services should provide evidence-based programs to address obesity and lack of exercise.	CBR	N/A
All mental health services should provide evidence-based programs to help smokers to quit.	CBR	N/A
Ensure that regular dental care is provided.	CBR	N/A

Medications for obesity in schizophrenia

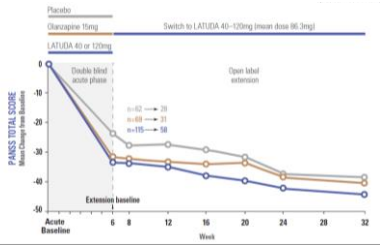
- Select antipsychotic or switch
- Augmenting strategies:
  - sibutramine (5HT / NA reuptake inhibitor) /orlistat (inhibits gastric lipases)
  - Topiramate (anticonvulsant), Nizatidine (H2 blocker) – small trials of some promise
  - Metformin – successful trials with olanzapine
  - Aripirazole – adjunctive to clozapine
  - Melatonin – RCT vs PBO

Weight loss in Patients switched from olanzapine to Latuda



Adapted from Stahl S et al J Clin Psychiatry 2013; 74: 507–15 and Data on file
Main analytical approach was on safety and tolerability
p values not reported

Efficacy maintained when switched from olanzapine to Latuda



Adapted from Stahl SM et al American Psychiatric Association 2012; Poster NR6-54
Main analytical approach was on safety and tolerability
p values not reported

RANZCP – Management strategies for metabolic adverse events

1. Galletly C, et al. *Aust N Z J Psychiatry*. 2016;50(5):410-472. (Table 8)

What do Australian Psychiatrists Think? (Laugharne et al, 2015)

Survey of 955 Fellows

- 80% thought metabolic monitoring was their responsibility
- 55% no established metabolic monitoring
- 13% didn't know what to monitor
- Under 50% checked weight, glucose, lipids
- Under 30%checked bp
- Under 7% checked waist circumference

Implementation of Metabolic Monitoring

Bridget Organ

Manager Community and Primary Mental Health

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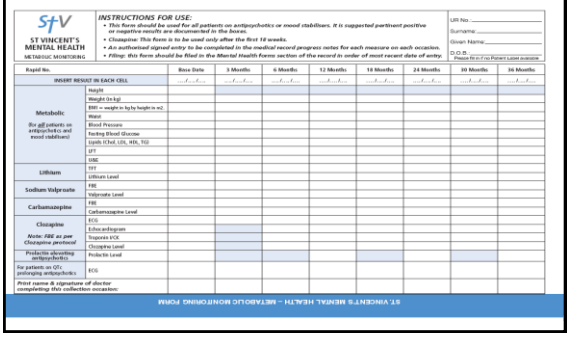
Form



ST VINCENT'S MENTAL HEALTH METABOLIC MONITORING

INSTRUCTIONS FOR USE:

- *This form should be used for all patients on antipsychotics or mood stabilisers. It is suggested pertinent positive or negative results are documented in the boxes.*
- *Clozapine: This form is to be used only after the first 18 weeks.*
- *An authorised signed entry to be completed in the medical record progress notes for each measure on each occasion.*
- *Filing: this form should be filed in the Mental Health Forms section of the record in order of most recent date of entry.*

UR No. _____ Surname: _____ Given Name: _____ D.O.B. _____ Please fill in if no Patient Label available

Rapid No.		Base Date	3 Months	6 Months	12 Months	18 Months	24 Months	30 Months	36 Months
INSERT RESULT IN EACH CELL		…/…/…	…/…/…	…/…/…	…/…/…	…/…/…	…/…/…	…/…/…	…/…/…
Metabolic (for all patients on antipsychotics and mood stabilisers)	Height								
	Weight (in kg)								
	BMI = weight in kg by height in m2								
	Waist								
	Blood Pressure								
	Fasting Blood Glucose								
	Lipids (Chol, LDL, HDL, TG)								
	LFT								
	UAE								
Lithium	EFT								
	Lithium Level								
Sodium Valproate	FBE								
	Valproate Level								
Carbamazepine	FBE								
	Carbamazepine Level								
Clozapine Note: FBE as per Clozapine protocol	ECG								
	Echocardiogram								
	Troponin ECK								
	Clozapine Level								
Protactin elevating antipsychotics	Prolactin Level								
For patients on QTc prolonging antipsychotics	ECG								

Print name & signature of doctor completing this collection occasion:

ST VINCENT'S MENTAL HEALTH – METABOLIC MONITORING FORM

Fact Sheet

Medical Morbidity in People with a Mental Illness

Guidelines for Staff:

Fact Sheet

Implementation Issues

- **who's job is it?**
- **how do we involve GPs?**
- **recording the results**
- **monitoring the monitoring at clinical review**
- **guidelines formalised**
- **outcomes encouraging (apart from waist circumference!) but need ongoing attention to maintain**

Implementation Issues

- **Really need dedicated (funded!!) staff working within mental health services:**
  - Australian study (McKenna et al, 2014)
  - US study (Druss et al, 2017)

Target Group

- People aged 18-60 with a diagnosis of psychosis
- Current cigarette smoker
- Body Mass Index (BMI) of >30
- Informed consent
- Willing to attempt to make some change in their smoking, diet, and level of physical activity

Results

- Four sites: 43 participants with schizophrenia/schizoaffective disorder
- Treatment sessions:
  - < 5 sessions = 5 (11.6%)
  - 5-8 sessions = 2 (4.7%)
  - All 9 sessions = 36 (83.7%)
- Follow-up assessment:
  - 43 participants (100%!)

Smoking Results

- A significant decrease in the number of cigarettes smoked over time
  - 30.8 cig/day to 17.2 cig/day, p=.0001
- Smoking status:
  - No change or increase = 16%
  - Less than 50% reduction = 35%
  - 50% reduction or more = 49%
- No cigarettes in past week = 19%
- Not a single cigarette since QUIT date = 12%

Weight Results

- Non-significant decrease in weight over time
  - 101kg to 99kg, p=.014
- Non-significant decrease in BMI over time
- Weight status:
  - No change or weight gain = 46%
  - Up to 5% reduction in body weight = 33%
  - More than 5% reduction in body weight = 21%
- Significant improvement in Quality of Life related to Weight

Exercise Results

- Almost significant increase in number of exercise sessions per week over time
  - 3.3 times to 4.8 times/week, p=.003
- Significant increase in the frequency of moderate exercise sessions over time
  - 2.4 times to 3.4 times/week, p=.001

Cardiovascular Risk Results

- Significant decrease in Overall Coronary Risk Percentile over time
  - 74 to 64, p=.001
- Fewer participants with an Overall Coronary Risk Percentile > 80 at follow-up:
  - 55% vs 42%

Conclusions

Patients with schizophrenia will spend more time in primary care
GPs will prescribe long term antipsychotics
Antipsychotics have significant side effects
Some are worse than others
The side effects cause significant morbidity and mortality
BUT
They can me minimised and they are treatable
There is a need for screening and intervening