Appendix 2

GUIDELINE ON MONITORING PSYCHOTROPIC PRESCRIBING IN RELATION TO CARDIOVASCULAR DISEASE

1. Background

The purpose of this guideline is to provide pragmatic advice to clinicians on lowering the risk of cardiac arrhythmia during treatment with psychotropic medication. A national CQUIN on 'Improving physical healthcare to reduce premature mortality in people with severe mental illness further reinforces these requirements.

1.1. Cardiac effects of psychotropic medication.

Adverse cardiac outcomes, particularly life threatening arrhythmias (torsade de pointes) and sudden death, are associated with a range of psychiatric medications for psychosis and depression. The main mechanism is prolongation of the QTc interval which is a risk factor for ventricular arrhythmias. Anti-psychotic medications differ in their propensity to induce QT prolongation, but most effects are dose related.

Drug-induced QTc prolongation is not inevitably related to risk of arrhythmia but arrhythmia is more likely to occur when other risk factors are present, predominantly pre-existing cardiovascular disease.

Clozapine is also associated with cardiomyopathy and myocarditis, particularly in the first few months of treatment. The risk may be as high as 1 in 1000 patients. The ECG may show ST depression but patients should also be monitored for symptoms and signs of heart failure.

1.2. Other drug factors

Many non-psychiatric drugs are associated with QTc prolongation and can exacerbate the effect of psychiatric medication. Examples include antibiotics, anti- arrhythmics, anti-malarials, methadone and tamoxifen.

Drug interactions can also exacerbate impact on QTc, for example, cytochrome p450 inhibitors and inducers, and potassium and magnesium wasting diuretics.

Rapid tranquillisation and use of high dose antipsychotics also increases risk of dangerous arrhythmia.

1.3. Patient factors

Patients with serious mental illness have a high prevalence of cardiac risk factors, including smoking, lack of exercise, obesity, substance misuse and diabetes. Cardiovascular disease is the most significant modifying variable for anti-psychotic induced sudden death. Other key risk factors for serious arrhythmia following psychotropic medication include:

- Long QT syndrome (and family history of LQTS or sudden death)

- Bradycardia
- Hypokalaemia, hypomagnesaemia and hypocalcaemia.
- Starvation
- Female gender and age over 70 years.

(Note: Brugada syndrome is an inherited condition affecting the cardiac sodium channel and can lead to syncope or sudden death. Characteristic ECG changes may be present all the time - coved ST elevation in V1 and V2, descending to an inverted T wave, resembling RBBB or may be unmasked by treatment with lithium or TCAs.)

1.4. Current standards

NICE guidelines advise baseline and follow up ECGs when prescribing anti- psychotic medication for inpatients or those with cardiovascular risks.

In addition, the SPCs (Summary of Product Characteristics) of a number of psychiatric medications specify the need for an ECG. The SPC is a legal document approved as part of the marketing authorisation of each medicine and is the definitive description of the product in terms of its properties and the clinical use to which it can put; a clinician would need strong grounds to ignore this advice.

Parity of esteem – meaning valuing mental health equally with physical health – is a key principle and priority in all national policies. Action to address (lack of) parity of esteem should include appropriate and proportionate attention to the physical health consequences of psychiatric medication.

2. Proposed pathway / algorithm

2.1. This pathway focuses on the specific role of ECG with respect to cardiovascular risk factors and prescribing psychiatric medication. The pathway is summarised in Figure 1. A comprehensive physical assessment is set out in:

- Trust Physical Healthcare Clinical Guideline
- The Mental Health Formulary and Prescribing Guidelines
- Assessment of lifestyle cardiovascular risks (smoking, diet and exercise) is included in the Care Programme Approach (CPA) documentation.

2.2. Baseline ECG is required before prescribing psychotropic medication if any one of the following risk factors are present:

- The patient has a history, symptoms or signs of established or occult cardiovascular disease;
- If there are independent vulnerability factors (family history, poly-pharmacy, potential drug interactions, disordered electrolytes);

- If a higher risk medication is essential to care (see Table 1).

If there are no risk factors and a lower risk medication is being prescribed, the patient should have routine clinical care, including an annual health check.

2.3. Correct modifiable risk or vulnerability factors:

- Review existing medication risks – poly-pharmacy and drug interactions;
- Correct abnormal electrolytes;
- Ensure known cardiac disease is under appropriate follow-up;
- Respond to wider health concerns as identified in the comprehensive physical health assessment.

2.4. Abnormalities in the baseline ECG should be discussed with the responsible primary care team and cardiology referral considered for serious ECG abnormalities.

2.5. Follow up ECGs is indicated:

- After steady state medication is reached;
- After a change in medication, a change in dose or poly-pharmacy;
- Change in risk status of the patient;
- Annually for patients on high dose medication or prescribed more than one anti-psychotic drug.

2.6. Enhanced clinical care is indicated in patients with ECG abnormalities or cardiovascular risk factors, including;

- Liaise with primary care team
- Consider changing psychotropic medication
- Be alert to drug interactions
- Monitor electrolytes
- Treat modifiable risk factors

2.7. Consider referral to cardiologist if significant ECG abnormalities are present:

- Prolonged QTc > 500 ms
- Any conduction abnormality apart from RBBB
- Bradycardia < 50 bpm
- ST segment deviation or abnormal T wave morphology
- Pathological Q waves.
- Voltage criteria for Left ventricular hypertrophy

Figure 1: Pathway to manage cardiovascular risks associated with psychiatric prescribing

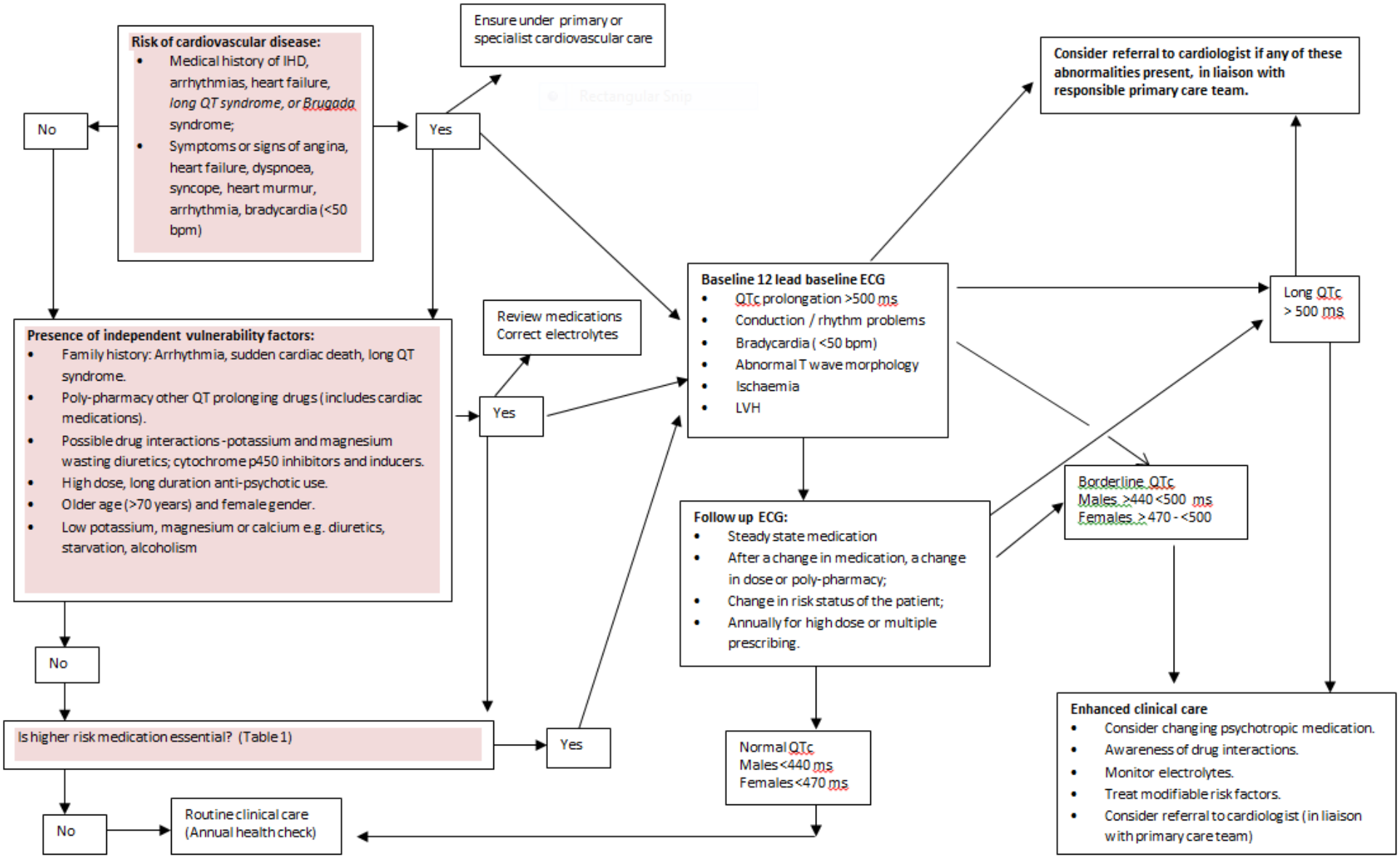

Table 1: Psychotropic medication by reported risk of induction of cardiac arrhythmia

(Medications in italics are not approved in the Trust formulary. Shaded medications are both approved in the Trust formulary and require an ECG as stated in the SPC)

	SPC – ECG recommendation. (note 2)	**Maudsley Prescribing guidelines 12th edition (note 3)**	**Weighted risk for cardiac arrhythmia (note 4)** (Fanoe et al., 2014)
Typical anti-psychotics			
Haloperidol	Yes	Moderate effect	B*
Chlorpromazine	Yes	Moderate effect	B
Flupentixol	No	Low effect	B
Perphenazine	No (consider with polypharmacy	Low effect	A
Sulpiride	No	Low effect	B
Trifluoperazine	No	Unknown effect	
Zuclopenthixol	No	Unknown effect	A
Fluphenazine decanoate	Yes	Low effect	
Carbamazepine	No	No effect	A
Benperidol	*Yes*		
Levomepromazine	*Yes*	Moderate effect	*B*
Pericyazine	*Yes*		
Pimozide	*Yes*	*High effect*	*B**
Prochlorperazine	*Yes*	*Low effect*	
Promazine hydrochloride	*Yes*		
Atypical antipsychotics			
Risperidone	No	Low effect	B
Amisulpride	Yes	Moderate effect	B
Aripiprazole	No	No effect	A
Clozapine	Yes	Low effect	B
Olanzepine	No	Low effect	A
Quetiapine	No	Moderate effect	B
Paliperidone	*No*	*Low effect*	*B*
Mood stabilisers			
Lithium	Yes	Low effect	B*
Asenapine	No	Low effect	A
Valproate	No	No effect	A
Lamotrigine	No	No effect	A

	SPC – ECG recommendation. (note 2)	**Maudsley Prescribing guidelines 12th edition (note 3)**	**Weighted risk for cardiac arrhythmia (note 4)** (Fanoe et al., 2014)
Approved drugs for depression in adults			
TCA			
Trazodone	The SPCs of TCAs urge caution, particularly in elderly, those with cardiac risks, potential drug interactions and overdose. However, ECG not specified for asymptomatic people.	Low effect	
Lofepramine		Moderate effect	
Imipramine		Moderate effect	B
Dosulepin		Moderate effect	
Amitriptyline		Moderate effect	B
Nortryptyline		Moderate effect	
MAOI			
Phenelzine	No	No effect	
Moclobemide	No	Low effect	B
Clomipramine	Yes	No effect	B
SSRI			
Sertraline	No	No effect	A
Paroxetine	No	No effect	A
Citalopram	Yes	Moderate effect (and dose related)	B
Escitalopram	Yes	Moderate effect (and dose related)	
Fluvoxamine	No	No effect	
Fluoxetine	Yes	No effect	A
SNRI			
Venlafaxine	No	Low effect	B
Duloxetine	No		A
NaRI			
Reboxetine	No	No effect	
NaSSa			
Mirtazapine	No	No effect	A
Busprione	No		
Methadone	Yes	QT prolonged	B*

Notes:

1. Drugs in italics are not on the EPUT approved formulary list.
2. SPC recommendation for ECG as of June 2017.

(Consult http://beta.medicines.org.uk/emc/search for up-to-date advice.)

Note, even when the SPC does not specify the need for a baseline or monitoring ECGs, they frequently urge caution when prescribing a psychiatric drug in a person with established cardiac disease or in comb

known to affect the QT interval.

3. Maudsley prescribing guidelines (12th edition) creates five categorises of risk of effect on prolonging QTc: No effect; low effect; moderate effect; high effect; unknown effect. (Note, prolonged QTc does not equate directly to risk of arrhythmia.)
4. Weighted risk recommendations for induction of cardiac arrhythmia.

A – drug considered without risk of QT prolongation
B – drug with a propensity of inducing QT prolongation
B* - drug with pronounced QT prolongation, or risk of TdP or serious arrhythmia. (Fanoe, S., Kristensen, D., Fink-Jensen, A., Jensen, H. K., Toft, E., Nielsen, J., Bundgaard, H. (2014). Risk of arrhythmia induced by psychotropic medications: a proposal for clinical management. European Heart Journal, doi:10.109. doi:10.1093/eurheartj/ehu100)

Notes:
Current policy requires

- Exec Med Director to audit adherence 3 yearly and report to clinical governance committee.
- Operations to audit policy quarterly on wards and annually in community.