QT prolongation is listed as a contraindication and adverse effect for many drugs commonly prescribed in older people in residential care. Older persons and females are at highest risk for this cardiac condition, most often caused by a combination of certain medications and various risk factors. QT prolongation can predispose to potentially fatal ventricular arrhythmias known as torsades de pointes.

**ECG**
An electrocardiogram (ECG) is a diagnostic tool that measures and records the electrical activity of the heart that results when the heart muscle cells in the atria and ventricles contract. One complete heartbeat in the ECG is described as a P-wave, QRS complex, and a T-wave. Atrial contractions show up as the P wave (depolarisation). Ventricular contractions show as a series known as the QRS complex. The third and last common wave in an ECG is the T wave. This is the electrical activity produced when the ventricles are recharging for the next contraction (repolarisation). QT prolongation is a measure of delayed ventricular repolarisation.

**QT prolongation**
The QT interval is an important component of an ECG. It is a measure of the time between the start of the Q wave and the end of the T wave in the heart’s electrical cycle. The QT interval varies considerably and is affected by age, gender and genetic factors. Congenital prolongation carries a high risk of sudden cardiac death.

The QT interval also varies with heart rate. The QT interval corrected for heart rate is called the QTc interval. The QTc interval is reported on the ECG printout.

**Torsades de pointes**
QT prolongation is associated with torsades de pointes and sudden cardiac death. Torsade de pointes usually stops spontaneously but frequently recurs, and may degenerate into ventricular fibrillation. Ventricular fibrillation is a life-threatening cardiac arrhythmia. Symptoms of cardiac arrhythmias include dizziness, palpitations and syncope.

The following is a list of factors associated with an increased tendency toward torsades de pointes with drug-induced QT prolongation:
- Genetic predisposition
- Bradycardia
- Heart failure
- Hypokalaemia
- Hypocalcaemia
- Hypomagnesaemia
- Hypothyroidism
- Hypothermia
- Anorexia
- Hepatic and renal impairment

Most cases of QT prolongation and torsades de pointes occur in the presence of one or more of these risk factors and certain medications. Residents should be assessed for these risk factors before being started on a QT-prolonging drug.

**Drug-induced QT prolongation**
Drugs are the commonest cause of QT prolongation. In general, the risk of drug-induced QT prolongation is directly related to the dose and plasma concentration of the drug. Over the last decade or so, many drugs commonly used in older people have been taken off the market due to concerns about QT prolongation and sudden cardiac death. This includes the antipsychotic thioridazine (Melleril), prokinetic agent cisapride (Prepulsid) and over-the-counter antihistamines astemizole (Hismanal) and terfenadine (Teldane).

Medicines that can cause QT prolongation include:
- Antifungals - fluconazole
- Antimotility agents - domperidone
- Antiarrhythmics - amiodarone, sotalol
- Antidepressants - amitriptyline, citalopram, escitalopram, fluoxetine, imipramine, doxepin
- Antipsychotics - chlorpromazine, haloperidol, lithium, olanzapine, quetiapine, risperidone, ziprasidone
- Macrolide antibiotics - erythromycin, clarithromycin, azithromycin
Quinolone antibiotics – moxifloxacin
Methadone

Of special note is citalopram (Cipramil), a selective serotonin reuptake inhibitor (SSRI) indicated for the treatment of major depression. It is commonly prescribed, partly because of its low potential for drug-drug interactions compared with other SSRIs such as fluoxetine (Prozac) and fluvoxamine (Luvox). In 2012 the recommended maximum daily dose of citalopram was reduced to 40 mg daily, due to reports of dose-dependent QT prolongation. In addition, people aged over 65 years of age, those with hepatic dysfunction, or taking medicines such as omeprazole (Losec) should only have a maximum dose of 20 mg daily. The recommended starting dose in the elderly is 10 mg daily. Citalopram is also contraindicated in patients with congenital long QT syndrome.

Some drugs such as amiodarone may cause QT prolongation, but rarely, if ever, causes torsades de pointes. Other drugs listed above such as quetiapine, venlafaxine and risperidone have a very low risk of torsades de pointes.

Erythromycin has been shown to prolong the QTc interval and is associated with case reports of torsades de pointes in some patients. Clarithromycin should not be given to patients with history of QT prolongation or ventricular cardiac arrhythmia, including torsades de pointes.

Domperidone (Motilium) is a medicine used for relief of symptoms of nausea and vomiting, and delayed stomach emptying. Recent reports have suggested domperidone should be used at the lowest effective dose for the shortest time possible. Domperidone should not be used with medicines that prolong QT interval or with medicines that inhibit CYP3A4. Additionally, domperidone should not be used in patients with moderate to severe hepatic impairment.

Drug interactions
Certain combinations of drugs resulting in drug interactions can contribute to torsades de pointes risk. Both pharmacokinetic and pharmacodynamic interactions can cause QT prolongation.

Drug-drug interactions that inhibit drug metabolism may increase the plasma concentration of the affected drug and precipitate QT prolongation. This is a pharmacokinetic interaction. For example, erythromycin and clarithromycin are commonly prescribed antibiotics, metabolised by CYP3A4. Calcium-channel blockers such as diltiazem and verapamil are potent inhibitors of CYP3A4 and when used in combination with these antibiotics can increase the risk of QT prolongation.

Pharmacodynamic interactions occur when two drugs have an additive effect. For example, concomitant use of escitalopram (Lexapro) and sotalol (Sotacor) is known to increase the risk of QT prolongation and torsades de pointes.

Diuretics can interact with QT prolonging drugs by causing electrolyte disturbances such as hypokalaemia and hypomagnesaemia.

Grapefruit juice can increase the risk of drug-induced QTc prolongation by inhibiting the metabolism of amiodarone.

Summary
Many commonly used drugs can prolong the QTc interval, especially when used in combination with other drugs which affect their metabolism. The risk of QT prolongation (which can be fatal) should be considered when weighing the risks and benefits of certain medicines. People taking other medications known to prolong the QT interval may be more susceptible to drug-associated effects on the QT interval. Residential Medication Management Reviews (RMMRs) by pharmacists can identify patients at greater risk for QT prolongation and life-threatening torsades de pointes.

References