# PHYSICAL HEALTH CHECKS IN PATIENTS ON ANTIPSYCHOTIC MEDICATION

Gloria Lau<sup>1</sup>, Juliette Murphy<sup>1</sup>, Natasha Chaudhury<sup>1</sup> & Mark Agius<sup>2</sup>

<sup>1</sup>School of Clinical Medicine, University of Cambridge, Cambridge, UK

<sup>2</sup>Centre for Mental Health Research in Association with the University of Cambridge, Cambridge, UK

#### **SUMMARY**

Schizophrenic patients have traditionally suffered from high rates of cardiovascular disease and early mortality. NICE guidelines suggest that several physical health measures be monitored regularly in these patients, and particularly those on antipsychotic medication, which has a wide side-effect profile that may potentiate the risk of cardiovascular disease and other comorbidities. This general practice audit aimed to determine the rates of physical health monitoring in primary care in patients on antipsychotic medication for over a year for psychotic symptoms or schizophrenia. The search was conducted in three different general practices in March 2019, yielding 19, 8 and 30 patients respectively, with a total of 57 patients.

This audit aims to record and analyse rates of monitoring of a range of physical health measures recommended by NICE guidelines over the past year. The results demonstrated that physical health monitoring was poor amongst all the practices audited, especially that of prolactin and waist circumference. We recommend that these rates of monitoring be improved, through implementing templates or the delivery of targeted education to general practitioners and nurses.

**Key words:** audit - antipsychotic medication - cardiovascular side effects - cardiovascular risk – psychosis – schizophrenia - hyperprolactinaemia

#### \* \* \* \* \*

# **INTRODUCTION**

Patients suffering with schizophrenia have long been known to be a disadvantaged group, with a shorter life expectancy than the general population (Šimunović Filipčić & Filipčić 2018), and higher rates of cardiovascular disease, which have remained elevated over the last decade (Rødevand et al. 2019).

Furthermore, this population is also at higher risk of diabetes, obesity and suicide (Cordes et al. 2017). Therefore, physical health monitoring plays an important role in identifying individuals with or at risk of cardiovascular disease or metabolic disorders, and modulating this risk.

NICE recommends that schizophrenic patients undergo an annual health check that is comprehensive, including weight, waist circumference, pulse and blood pressure, fasting blood glucose, HbA1c, blood lipid profile. An assessment of nutritional status, diet and level of physical activity is also to be noted ('Psychosis and schizophrenia in adults: prevention and management | NICE Guidance').

These checks are particularly important for those on antipsychotic medication, which improve outcomes for patients (Stafford et al. 2015). However, this class of medications may lead to many and varied side effects including extrapyramidal symptoms, hyperprolactinaemia, sexual dysfunction, cardiovascular side-effects, hypotension, hyperglycaemia and weight gain (Wolfgang & Ukok, n.d.). For this reason, the BNF recommends that monitoring of full blood count (FBC), urea and electrolytes (U&Es), liver function tests (LFTs), blood lipids, fasting blood glucose, and blood pressure is required at least annually after the antipsychotic is prescribed.

These particular physical health measures, recommended by both NICE and the BNF, play a key role in monitoring the varied side effects of antipsychotic medication, and thus preventing poor health outcomes for affected individuals. For instance, FBC must be monitored regularly as clozapine may cause agranulocytosis which can lead to sepsis and death (Węclewicz & Wiciński 2018). U&Es and LFTs must be regularly measured as antipsychotic use can result in derangements in electrolyte balance (Yang et al. 2018) and liver function, with the risk of rare but severe hepatic injury (Marwick et al. 2012).

Antipsychotic use may also lead to an elevation in prolactin levels, which can cause gynaecomastia, galactorrhoea, infertility and amenorrhoea (Haddad & Wieck 2004). These effects are little researched in psychiatric patients, but highly prevalent, with some studies reporting prevalence rates of up to 45% for amenorrhoea in women treated with conventional antipsychotics (Peuskens et al. 2014). The effects of hyperprolactinaemia include long term osteoporosis, a recognised cause of significant morbidity. Although at present there are few studies looking at the effects of osteoporosis in psychiatric patients, the potential for deleterious long-term consequences of antipsychotic medication cannot be ignored and should reinforce the need for adequate monitoring of prolactin in these at risk groups.

Furthermore, an increased risk of developing type II diabetes mellitus with antipsychotic use (Whicher et al.

2018) is evident, especially with commonly used atypical antipsychotic agents such as olanzapine. As such, fasting blood glucose and HbA1c must be monitored to identify those at risk of diabetes early, in order to slow or halt progression through conservative measures, or else control the condition to prevent serious complications, such as peripheral neuropathy, nephropathy and retinopathy (Faselis et al. 2019).

Atypical antipsychotic medication use increases the risk of metabolic syndrome, including a rise in obesity (Mahendran et al. 2010) and hyperlipidaemia (Mhalla et al. 2018), another risk factor for cardiovascular disease. Blood lipid levels, weight, and waist circumference (a more accurate marker of cardiovascular disease risk than BMI) (Savva et al. 2010) should therefore be monitored annually. Blood pressure should also be monitored as there is a high prevalence of hypertension in the schizophrenic population (Bushe et al. 2005). Lifestyle advice is crucial in modifying these cardiovascular disease risk factors, including advice about diet and exercise.

Given the elevated risk of cardiovascular disease and early mortality in schizophrenic patients, alongside the side effects of antipsychotics which may further increase this risk, it is clear that careful physical health monitoring of this population is crucial in improving their long-term health outcomes. According to NICE guidelines ('Psychosis and schizophrenia in adults: prevention and management | Guidance | NICE') primary care should monitor the physical health of patients with psychosis or schizophrenia when the responsibility is transferred from secondary care, and then at least annually. This audit aims to look at patients who have been on antipsychotic medication for at least a year to treat symptoms of schizophrenia or psychosis, in order to determine the rates of monitoring in primary care.

# METHODS

The populations of three general practices were searched on practice computers using SystmOne for patients meeting the audit search criteria.

### Search criteria

'Antipsychotic medication' for over 1 year AND 'Psychotic disorder' or 'Schizophrenia'.

This search was conducted in March 2019 in yielding 19, 8 and 30 patients at practice 1, 2 and 3 respectively, with a total of 57 patients.

Once this cohort of 57 patients had been identified, their patient notes were manually searched for evidence of physical health monitoring in the last 12 months, as specified by NICE guidelines. This evidence included recordings of full blood count (FBC), urea and electrolytes (U&Es), liver function tests (LFTs), blood lipids, glucose measurements (including HbA1c and fasting blood glucose), and prolactin. In addition to these measurements, the patient notes were searched for measurements of weight, waist circumference, blood pressure and pulse, as well as for records of lifestyle advice given to the patient.

# RESULTS

The results demonstrate heterogeneity in monitoring across all three practices. For example, practice 2 achieved a 75% rate of recording lifestyle advice given to patients, while practices 1 and 3 recorded a much lower percentage of patients to whom lifestyle advice had been given in any context. Fasting blood glucose was only monitored in 5.3% of patients in practice 1, whereas practice 2 and 3 achieved monitoring of 62.5% and 40% of their patients' fasting blood glucose respectively (Table 1, Figure 1).



Figure 1. Physical Health Monitoring of Patients on Antipsychotic over the Past Year

Gloria Lau, Juliette Murphy, Natasha Chaudhury & Mark Agius: PHYSICAL HEALTH CHECKS IN PATIENTS ON ANTIPSYCHOTIC MEDICATION Psychiatria Danubina, 2019; Vol. 31, Suppl. 3, pp 608-612

Table 1. Physical Health Monitoring												
Physical Health Measure	FBC	U&Es	LFTs	Blood lipids	HbA1c	Fasting blood glucose	Prolactin	Weight	Waist Circumf erence	BP	Pulse	Lifestyle advice
Practice 1	47.40%	57.90%	52.60%	31.60%	47.40%	5.30%	10.50%	73.70%	15.80%	94.70%	42.10%	31.60%
Practice 2	62.50%	62.50%	75.00%	62.50%	37.50%	62.50%	0.00%	75.00%	62.50%	75.00%	50.00%	75.00%
Practice 3	36.70%	66.70%	46.70%	63.30%	53.30%	40.00%	6.70%	66.70%	6.70%	73.30%	50.00%	33.30%
Total	43.90%	66.70%	52.60%	52.60%	49.10%	31.60%	7.00%	70.20%	17.50%	80.70%	47.30%	38.60%



Practice 1 Practice 2 Practice 3

Figure 1. Physical Health Monitoring of Patients on Antipsychotic over the Past Year - 3 practices

The overall rate of physical health monitoring of the 57 patients from the 3 practices on antipsychotic medication for psychotic symptoms or schizophrenia is extremely low, with no single physical health measure being monitored in 100% of patients in the past year. Across all three practices, the most well recorded measure was blood pressure, while the least well recorded measure was prolactin (Figure 2).

The variation demonstrated in these results, both across physical health measures and across practices, highlights the need for a more uniform and regimented approach to monitoring in this cohort of patients.

#### DISCUSSION

This audit found that, across three different GP practices, patients on antipsychotics were not being adequately monitored for physical health changes as recommended by NICE guidelines. Although it is recommended that patients are monitored annually, this audit found that none of the physical health measures were being monitored in 100% of the patients and, furthermore, that the rates of monitoring the different measures varied from practice to practice.

The results demonstrate low rates of monitoring, despite the adverse health outcomes and high rates of mortality experienced by patients suffering from schizophrenia (Andor et al. 2019). Schizophrenia is associated with a greater cardiovascular risk, which could be secondary to both the disease as well as the high level of cardiovascular risk factors associated with that patient population The life expectancy is approximately 13-30 years shorter amongst patients with schizophrenia (Andor et al. 2019). This difference in mortality is assumed to be due to other comorbidities, such as cardiovascular disease, diabetes, and poor monitoring of other risk factors. Thus monitoring of modifiable risk factors and regular follow ups and lifestyle advice with such patients could prevent this disparity in life expectancy (Eich & Nick 2008).

Furthermore, schizophrenic patients have a greater chance of dyslipidaemia (Mhalla et al. 2018), yet 52.6% of the total patients were sent for blood lipid tests within the last year, with Practice 1 having the lowest percentage of checks at 31.6%.

Enforcing regular blood lipid checks is important in preventing future cardiovascular events. Lifestyle measures such as smoking cessation advice should furthermore be offered (Wilson et al. 2019).

Blood pressure and weight monitoring were more adequately monitored than the other measures across all three practices. This is perhaps partially because these measures were often recorded in GP attendances pertaining to other conditions and comorbidities, such as cardiovascular disease or diabetes. For instance, both blood pressure and weight monitoring are included in NICE Quality Outcomes Framework indicators. This encourages general practitioners to establish and maintain a register of patients aged 18 or over with a BMI >25 in the preceding 12 months (NICE id code: NM128), and to keep a record of patients' blood pressure for other disease monitoring and primary prevention.

Across all three practices, prolactin levels were systematically under-measured, with practices 1 and 3 monitoring under 10% of their patients, and practice 2 having no records of prolactin measurements in any of the cohort of patients. This is particularly concerning, as there are many studies linking the use of antipsychotics to high levels of prolactin, and this has been a recognised common adverse effect of antipsychotic medication since the 1970s (Peuskens et al. 2014). In order to prevent or identify the potential consequences of hyperprolactinaemia, which includes gynaecomastia, galactorrhoea, infertility and amenorrhoea, as well as osteoporosis, adequate monitoring of prolactin in these groups is crucial.

#### Recommendations

In order to address the heterogeneity in monitoring, and to increase overall rates of monitoring, we suggest creating and implementing a template on SystmOne to increase adherence, including all of these measures:

- FBC, U&Es, LFTs;
- Blood lipids;
- HbA1c;
- Fasting blood glucose;
- Weight;
- Waist circumference;
- Blood pressure;
- Pulse;
- Prolactin.

Overall physical health assessment, including comment on diet, exercise levels and overall function.

We recommend that practitioners should review patients and consider for psychiatric referral for altering of medication if the HbA1c rises above 42mmol/mol (6.0%), or fasting glucose above 5.5mmol/L, both which are indicators of pre-diabetes. This would help improve rates of primary prevention of metabolic syndrome which, as discussed above, has been found to be associated with antipsychotic use. In addition, lifestyle advice (including advice to stop drinking or smoking, and to control diet), and consideration of review should be given if one carries clinical suspicion of metabolic syndrome or risk of cardiovascular disease. For example, this might be considered after observing a significant increase in weight or blood lipid levels within a year. If the antipsychotic medication is found to be causing features of metabolic syndrome, the patient should be referred back to psychiatry to consider a change of medication. If it is decided that medication cannot be changed, then other modifiable risk factors for metabolic syndrome, such as cholesterol and hypertension, must be managed.

Furthermore, it may be beneficial to educate GPs and other primary healthcare professionals on the side effects of antipsychotic medication so that they better understand the reasons for which schizophrenic patients must be so closely monitored. This would improve adherence to the implementation of a regimented physical monitoring template, and thus improve patient outcomes.

# CONCLUSION

Much of the literature has corroborated the importance of primary prevention across many states of ill health, particularly cardiovascular disease, but further research is required concerning the importance of preventing this increased rate of mortality in patients receiving antipsychotic medication. However, the consensus seems to be that increased monitoring of physical health measures should be a priority for primary healthcare practitioners (Osborn et al. 2007).

This audit has identified particularly low levels of monitoring of prolactin in this cohort, and more consistent monitoring of blood pressure and weight. Therefore, there is scope for improvement of monitoring, which may be achieved through implementation of a template including all the required physical health measures. These changes will hopefully lead to primary prevention of causes of increased morbidity and mortality among this cohort of psychiatric patients, including reduced risk of cardiovascular disease and type 2 diabetes mellitus.

The results of this audit may be limited by the fact that the three practices were located in a similar geographical area, which may influence the results, reflecting local differences in practice. Additionally, several patients were noted to have not arrived for scheduled appointments, or to have refused blood testing. This limits the frequency of monitoring of these patients, and may explain, in part, why the results showed a discrepancy in rates of monitoring of different physical health measures, with simple testing that can be performed in the same appointment tending to have been carried out across a larger proportion of the cohort, compared with tests requiring a second appointment to be booked. In order to address these limitations, further auditing could be undertaken across a wider geographical range, and the rates of non-attendance for different types of appointment in this cohort of patients could be investigated.

The results demonstrate that rates of monitoring in patients receiving antipsychotic medication across three general practices were low across all measures. As previously discussed, such poor levels of monitoring of physical health in this cohort may have detrimental effects, stemming from a fundamental lack of identification of patients at risk of metabolic and other disease. The result is the advent of adverse health outcomes in what is already a disadvantaged group.

### Acknowledgements:

This audit was carried out as part of assigned coursework at the School of Clinical Medicine University of Cambridge.

Conflict of interest: None to declare.

#### Contribution of individual authors:

Gloria Lau developed the Audit Standards.

- Gloria Lau, Juliette Murphy & Natasha Chaudhury carried out the audit.
- Mark Agius supervised the analysis and writing up of the project.

# References

- Andor M, Dehelean L, Romosan A-M, Buda V, Radu G, Caruntu F, Tomescu M: A novel approach to cardiovascular disturbances in patients with schizophrenia spectrum disorders treated with long-acting injectable medication. Neuropsychiatric Disease and Treatment 2019; 15:349–355. https://doi.org/10.2147/NDT.S186892
- Bushe C, Haddad P, Peveler R & Pendlebury J: The role of lifestyle interventions and weight management in schizophrenia. Journal of Psychopharmacology (Oxford, England) 2005; 19(6 Suppl):28–35. https://doi.org/10.1177/0269881105058682
- 3. Cordes J, Bechdolf A, Engelke C, Kahl KG, Balijepalli C, Lösch C, Moebus S: Prevalence of metabolic syndrome in female and male patients at risk of psychosis. Schizophrenia Research 2017; 181:38–42.

https://doi.org/10.1016/j.schres.2016.09.012

- 4. Eich P & Nick B: Pharmacotherapy of schizophrenia spectrum disorders: State of the Art. TherUmsch, 2008
- Faselis C, Katsimardou A, Imprialos K, Deligkaris P, Kallistratos M & Dimitriadis K: Microvascular complications of type 2 diabetes mellitus. Current Vascular Pharmacology 2019. https://doi.org/10.2174/1570161117666190502103733
- Haddad PM & Wieck A: Antipsychotic-induced hyperprolactinaemia: mechanisms, clinical features and management. Drugs 2004; 64:2291–2314. https://doi.org/10.2165/00003495-200464200-00003
- 7. Mahendran R, Hendricks M & Chan Y: Weight gain in Asian patients on second-generation antipsychotics. Ann Acad Med Singapore, 2010

- 8. Marwick K, Taylor M & Walker: Antipsychotics and abnormal liver function tests: systematic review. Clinical Neuropharmacology, 2012
- 9. Mhalla A, Bel Hadj Salah W, Mensi R, Amamou B, Messaoud A, Gassab L, Gaha L: Lipid profile in schizophrenia: case control study. La Tunisie Medicale 2018; 96:22–29
- 10. Osborn D, Levy G & Irwin N: Relative Risk of Cardiovascular and Cancer Mortality in People With Severe Mental Illness From the United Kingdom's General Practice Research Database. Arch Gen Psychiatry https://doi.org/doi:10.1001/archpsyc.64.2.242
- 11. Peuskens J, Pani L, Detraux J & De Hert M: The effects of novel and newly approved antipsychotics on serum prolactin levels: a comprehensive review. CNS Drugs 2014; 285:421–453. https://doi.org/10.1007/s40263-014-0157-3
- 12. Rødevand L, Steen NE, Elvsåshagen T, Quintana DS, Reponen EJ, Mørch RH, Andreassen OA: Cardiovascular risk remains high in schizophrenia with modest improvements in bipolar disorder during past decade. Acta PsychiatricaScandinavica 2019; 139:348–360. https://doi.org/10.1111/acps.13008
- 13. Savva S, Tornaritis M, Savva M, Kourides Y, Panigi A, Silikiotou N, Kafatos A: Waist circumference and waist-toheight ratio are better predictors of cardiovascular disease risk factors in children than body mass index. International Journal of Obesity, 2010. Retrieved from https://www.nature.com/articles/0801401
- 14. Stafford MR, Mayo-Wilson E, Loucas CE, James A, Hollis C, Birchwood M & Kendall T: Efficacy and safety of pharmacological and psychological interventions for the treatment of psychosis and schizophrenia in children, adolescents and young adults: a systematic review and metaanalysis, 2015.
  - https://doi.org/10.1371/journal.pone.0117166
- 15. Węclewicz M & Wiciński M: Clozapine-induced agranulocytosis/granulocytopenia: mechanisms and monitoring. 2018
- Whicher CA, Price HC & Holt RIG: Mechanisms in endocrinology: Antipsychotic medication and type 2 diabetes and impaired glucose regulation. European Journal of Endocrinology 2018; 178:R245–R258. https://doi.org/10.1530/EJE-18-0022
- Wilson SM, Thompson AC, Currence ED, Thomas SP, Dedert EA, Kirby AC, Beckham JC: Patient-Informed Treatment Development of Behavioral Smoking Cessation for People With Schizophrenia. Behavior Therapy 2019; 50:395–409. https://doi.org/10.1016/j.beth.2018.07.004
- 18. Wolfgang G & Ukok A: Side effects of atypical antipsychotics: a brief overview. Official Journal of the World Psychiatric Association. (n.d.)
- Yang Q, Guo X & Liu D: Hypokalemia Caused by Quetiapine and Risperidone Treatment in Schizophrenia: A Case Report. Shanghai Archives of Psychiatry 2018; 30:204–206. https://doi.org/10.11919/j.issn.1002-0829.217168

Correspondence: Gloria Lau, MD School of Clinical Medicine, University of Cambridge Cambridge, UK E-mail: gloriayifang@gmail.com