



RCPI

MASTERCLASS

Meeting Report

Hearts & Minds:

Exploring the cardiovascular risk
burden in psychiatric disease

2nd - 3rd December 2005

RCPI, 6 Kildare St, Dublin 2



Introduction

Prof. T. Joseph McKenna, *President, RCPI*



The first in a series of educational meetings specifically designed to review topics of emerging interest or ongoing controversy under the broad title of "Masterclasses", was held in the Royal College of Physicians of Ireland on December 2nd-3rd 2005. This was also the first major educational meeting held in the College since its recent restoration, renovation and refurbishment. The disproportionate burden of cardiovascular disease carried by patients with psychiatric disorders was the focus of the meeting. This topic was prompted by the realisation that while this is a serious health problem within society, it is not widely recognised and the management response frequently ambivalent. The major concern is probably that patients already coping with a major disorder, might be psychologically overwhelmed by the demands of lifestyle change which are integral components of the management of cardiovascular disease and its prevention. Furthermore, there are possible problems arising from the prescription of potentially a wide array of medications in addition to those already prescribed for the mood disorder. The general implications of cardiovascular disease in psychiatric patients, the scale of the problem and models for addressing

the problem were expertly addressed during this two day meeting.

An outstanding panel of presenters was chosen by the Programme Faculty of College Fellows specifically convened for this meeting and they were entirely justified in all of their choices of titles and speakers. I would like to recognise and thank each Faculty Member; Dr. Ted Dinan, Dr. Sean Dinneen, Dr. John Feely, Dr. Kevin Malone, Dr. Seamus Sreenan and Dr. John Sheehan.

Delegates attended not only from Ireland and UK but also from Austria, Belgium, Czech Republic, Denmark, Estonia, Greece, Hungary, Latvia, Netherlands, Romania, Slovakia, Sweden, Switzerland. The general feedback was that this was a very helpful meeting and delegates brought back with them to their various countries the message that we are all not adequately addressing the problem of cardiovascular disease in patients with psychiatric disorders. It is hoped that this meeting will provide an impetus from which will grow institutional strategies and eventually national programmes to tackle this now obvious public health problem. The Royal College of Physicians of Ireland has been proud to play a role in highlighting the problem and in examining how it can be addressed. The College acknowledges the essential unrestricted educational grant provided by Bristol-Myers Squibb. The Royal College of Physicians of Ireland hopes that a future meeting will be able to report the impact of the initiatives being undertaken as a result of this first Masterclass.

Yours sincerely,

A handwritten signature in black ink, which reads "T. Joseph McKenna". The signature is written in a cursive style with a large initial 'T'.

Prof T Joseph McKenna
President, RCPI

Setting the Scene; The Burden of Obesity and Metabolic Syndrome; Cardiovascular Risk in Psychiatric Patients



Psychiatric and Cardiovascular Risk – The Problem Defined

By Prof Ted Dinan,
*Professor of Psychiatry,
Cork University Hospital*

The opening presentation was offered by Ted Dinan, Professor of Psychiatry in UCC. The focus was on the cardiovascular risk burden in two major psychiatric conditions – depression and schizophrenia. A number of studies have shown that psychiatric patients have a higher mortality from cardiovascular causes than the general population. For instance, Valliant's 1998 paper on a fifty-five year prospective study following medical students through their lives found that 45% of those who had had a psychiatric episode had died by the fifty-five year point while only 5% of those who had had good psychological health had died. The Longitudinal Ages Study Amsterdam (LASA) has shown that depression is associated with an excess risk of cardiac mortality in those with and without a baseline cardiac history. Those who had suffered major depression had twice the risk of those who had had a minor depressive episode. This risk is

not gender specific and is independent of lifestyle factors associated with depression.

As for schizophrenia, it is well known that premature mortality is increased in this condition. Total mortality is twice as high as in the general population and life expectancy is 20% shorter. In Salokangas et al's 2002 study, 4338 patients were prospectively followed post discharge. Physical illness was the commonest cause of death in the 5.2% who died. The biology of stress seems likely to play a role in increasing the risk of cardiovascular illness in psychiatric conditions and Professor Dinan discussed the HPA (Hypothalamic Pituitary Adrenal) axis and the role of cortisol in this regard.

Ted Dinan is Professor of Psychiatry at University College Cork. He was previously Chair of Clinical Neurosciences and Professor of Psychological Medicine at St. Bartholomew's Hospital, London. Prior to that he was a Senior Lecturer in Psychiatry at Trinity College Dublin. He has worked in research laboratories on both sides of the Atlantic and has a PhD in Pharmacology from the University of London. He is a Fellow of the Royal Colleges of Physicians and Psychiatrists and a Fellow of the American College of Physicians. He has published over 180 papers and numerous books on the pharmacology and neurobiology of affective disorders. His papers have been published widely in journals such as Nature, Brain Research, British Medical Journal, American Journal of Psychiatry, British Journal of Psychiatry and Clinical Endocrinology and Metabolism.



The Multifactorial Nature of Cardiovascular Risk

By Prof John Feely,
*Professor of Pharmacology and
Therapeutics, Trinity College Dublin,
Consultant Physician, St. James's
Hospital*

Professor Feely focused on atherothrombosis which of course is the common pathway for cardiovascular disease. A wide range of risk factors have been identified and explored – more than two hundred have been discussed in the literature. Most of these are well known and some are modifiable whilst others are not. One with an increasing evidentiary base is below average birth weight, particularly when associated with a 'catch up' of weight before the age of eleven. The Inter Heart Study has shown that there is an exponential increase in the risk of myocardial infarction with multiple risk factors. Blood tests that help predict morbidity have also been identified. C-Reactive Protein (CRP) shows particular promise.

Psychosocial stressors are also implicated. For instance, a study of English civil servants has shown that a sense of

"justice" in the workplace, and an internal locus of control, is protective. The "type D personality", which tends to conceal emotional stress, is also prone to myocardial infarctions. Concomitant depressed mood is, interestingly, shown to increase substantially the predictive power of CRP. Educational factors also play a part – in the United States, it has been shown that lacking high school education is associated with an average loss of thirteen years from life expectancy.

Professor Feely discussed the overall decline in coronary heart disease – a theme of many talks at the Masterclass. Smoking is in decline and cholesterol levels are also decreasing. However, a surge in obesity and type II diabetes threatens to reverse these gains. Screening for cardiovascular risk will remain important for a long time to come. While tests such as CRP have potential, the cornerstones of screening for cardiovascular risk remain blood pressure, weight, waist/hip ratio, smoking, glucose and lipid profile.

John Feely, a graduate of the National University of Ireland 1971, undertook his Pharmacology and General Internal Medicine Training in Dublin. He was subsequently appointed Senior Registrar in Medicine and Endocrinology at Ninewells Hospital, Dundee, Scotland. In 1979-81 he was a Merck International Fellow in Clinical Pharmacology at Vanderbilt University, Tennessee, USA and subsequently Lecturer at the University of Dundee. He was appointed Professor of Pharmacology and Therapeutics at Trinity College Dublin and Consultant Physician at St. James's Hospital, Dublin in 1983. He is currently the Director of the Hypertension and Lipid Clinics at St. James's Hospital and Medical Director of the National Medicines Information Centre. His research interests are in Cardiovascular Pharmacology, Hypertension, Arterial Stiffness, Lipids and Pharmacoepidemiology.

Setting the Scene; The Burden of Obesity and Metabolic Syndrome; Cardiovascular Risk in Psychiatric Patients



Metabolic Syndrome – An Emerging Epidemic

By Dr Sean Dinneen,
Consultant Endocrinologist,
University College Hospital, Galway

Worldwide, a conservative and probably obsolete WHO projection posits that there will be 221 million diabetics by 2010. The bulk of this increase will be in Asia, Africa and South America. Changes in diet and lifestyle amongst formerly diabetes-free populations have contributed to the emerging pandemic. While diabetes is increasing, pre-diabetic states are also vastly more common. Glucose intolerance in the obese is as common as diabetes itself. Insulin resistance is of itself associated with hypertension, dyslipidaemia, atherosclerosis and endothelial dysfunction. The American Diabetes Association has reduced the threshold for Impaired Fasting Glucose from 6.1 mmol/l to 5.6 mmol/l in recognition of this fact.

Metabolic syndrome has become the object of some controversy in endocrinological circles. The 2005 American Heart Association definition

gives a list of criteria; a waist circumference of more than 102 cm in men and 88 cm in women; elevated triglycerides; reduced HDL-C; elevated blood pressure (over 130 systolic or 85 diastolic or requiring medication); and elevated fasting glucose (above 5.6 mmol/l or requiring medication). Both American and European Diabetology Associations have called for a critical review of the condition. Gale in 2005 wrote that it is impossible to distinguish between the definition of the metabolic syndrome, the predictive power of the syndrome and its implications for treatment. They are, according to Gale, “all one and the same thing.”

The Diabetes Prevention Programme Group's report has affirmed that high risk patients can manage their risk. Lifestyle changes reduced risk by 58%. Metformin has a definite role to play and is most effective in younger or overweight participants.

Sean Dinneen received his medical degree from University College Cork Medical School. He undertook postgraduate training in medicine in Ireland and then went to the United States where he trained in Diabetes and Endocrinology at the Mayo Clinic. After a period on staff at the Mayo Clinic he was appointed as a Community Diabetologist in Addenbrooke's Hospital, Cambridge. He has recently returned to Ireland to take up a Senior Lecturer post in Medicine in University College Hospital, Galway. His professional interests are in delivering programmes of self-management education for people with diabetes and developing optimal models of community-based diabetes care.



Lipids – Current Understanding

By Dr Brendan Buckley,
Consultant Endocrinologist,
University College Cork

Of the many-headed beast that is cardiovascular risk, cholesterol is the central and crucial component because LDL cholesterol is fundamentally necessary for the formation of an atheromatous plaque.

Dr Buckley discussed how the necessity and safety of treating elevated cholesterol has gradually been established despite initial media frenzy which alleged that such treatment might cause violence and suicide. None of the wilder scare stories in this regard have been remotely borne out. In possibly the largest series of outcomes trials ever performed, statins have been shown to be highly effective in primary and secondary prevention of coronary disease. Based on epidemiological observations such as the Seven Countries Study and on interpretation of pooled statin trials, Dr Buckley also discussed the possibility that extreme lowering of cholesterol levels well below those hitherto regarded as “normal” for

Western European and North American populations might virtually eliminate cardiovascular events.

CONCLUSIONS

- LDL cholesterol is the main driver of atherosclerosis.
- Lowering plasma LDL levels has a major beneficial effect in risk reduction, even in people with advanced and long-established disease
- Some antipsychotic treatments may make dyslipidaemia worse.
- This will significantly increase cardiac risk.
- Selectivity in antipsychotic drug use can minimise this.

Brendan Buckley DPhil, FRCPI is Consultant Endocrinologist at Bon Secours Hospital Cork and faculty member in the Departments of Medicine and of Pharmacology & Therapeutics at University College Cork (UCC). He is the Director of the European Centre for Clinical Trials in Rare Diseases at UCC. He is the Director in Ireland of a number of large clinical trials, including the PROSPER Study, a major intervention trial in prevention of vascular disease in 5800 older adults using pravastatin as anti-atherosclerotic therapy. He has published extensively in the areas of metabolic disease and atherosclerosis. He is the Chairman of the Advisory Committee on Human Medicines of the Irish Medicines Board, and a member of the Board.

Setting the Scene; The Burden of Obesity and Metabolic Syndrome; Cardiovascular Risk in Psychiatric Patients



Hypertension – Current Understanding

By Dr Vincent Maher,
Consultant Cardiologist,
Adelaide and Meath Hospital, Dublin

Dr Maher challenged the audience to reconsider hypertension as a complication of a vascular disorder rather than vascular disorder being a complication of hypertension. In a thought provoking talk, he focused on the vasculopathy which underlies hypertension. Medical intervention only tends to occur when vascular pathology is symptomatic and therefore well advanced.

Dr Maher overviewed the principles underlying the pathophysiology, diagnosis and management of hypertension. Ambulatory blood pressure monitoring, rather than isolated readings, is crucial. The distinction between essential and secondary hypertension was discussed. The vast majority (90-95%) of patients with hypertension have essential hypertension. Dr Maher discussed the particular circumstances in which secondary hypertension is particularly

suspected – with readings over 180/110; with a renal bruit on examination; with associated hypokalaemia; with marked blood pressure variability; with the absence of a nocturnal dip on monitoring; and with refractory blood pressure unresponsive to three antihypertensives.

Of the 90-95% patients with hypertension who have the essential type, 65% have metabolic syndrome.

Obesity leads to a rise in leptin levels and an increased sympathetic drive, which further leads to a rise in Angiotensin II and a resulting rise in blood pressure. Alternative measurements, rather than the classic Korotkoff method, were discussed and these included serial ECGs to assess left ventricular hypertrophy or repeated twenty four hour urine collections to assess protein. Dr Maher suggested these would offer a better insight into the potential micro-vascular pathology which may precede hypertension on measurement.

The keynote of Dr Maher's speech was the importance of early intervention in hypertension. In response to questions from the floor, he discussed the doubtful value of once-off blood pressure measurements at the time of outpatient

visits in psychiatric patients and stressed that patients deserved 24 h ambulatory blood pressure monitoring and measures of vascular changes. Monitoring vascular change is the ideal way to assess ones efficacy in blood pressure treatment.

Vincent Maher graduated from UCG in 1981 and initially pursued a career in general medicine and specialized in Cardiology in Ireland. He became a member of the Royal College of physicians and completed the work for his MD joining the Cardiology Department at the Hammersmith hospital in London as an Honorary Senior registrar. Later he moved to the University of Washington in Seattle USA, where he trained in interventional cardiology and became a staff cardiologist and Assistant Professor. He returned to Ireland in 1998 as a consultant cardiologist and Medical Director of the Irish Heart Foundation. Recently Dr Maher has become the President of the Irish Hyperlipidaemia Association and the Vice President of the Irish Association of Cardiac Rehabilitation. His main areas of interest are in Vascular monitoring, hypertension and reversal of coronary artery disease.



Diabetes – The Global Cardiovascular Challenge

By Dr Amanda Adler,
Consultant Physician,
Addenbrookes Hospital, Cambridge, UK

Diabetes is associated with an overall two-fold increased risk of cardiovascular disease, and a three- to four-fold increase for women. Cardiovascular disease is the most common complication of type 2 diabetes. In the absence of diabetes, cardiovascular disease is more common the higher the HbA1c, a measure of glycaemia. Amongst patients with type 2 diabetes, A one per cent decrease in HbA1c would be expected to reduce the risk of myocardial infarction by approximately 14%, and is in keeping with the UKPDS study's findings. Blood glucose lowering with metformin in the UKPDS lowered the risk of myocardial infarction by approximately one-third. Metformin is not only effective, but also cost effective and likely to be cost-saving due to the low price of metformin and the high price of treating cardiovascular disease.

Amanda Ingham Adler, MD, PhD, FRCP, trained in economics, epidemiology and medicine. She worked as a diabetes epidemiologist in Seattle, Washington and for the Indian Health Service in the Alaskan arctic prior to moving to Oxford University as an epidemiologist and investigator on the UK Prospective Diabetes Study (UKPDS). Dr. Adler has consulted with the US Health Service Task Force, the World Health Organisation, the UK Medical Research Council, and the UK National Screening Committee with respect to screening and treatment of diabetes.

Currently, in addition to her role as Research Associate, Diabetes Trials Unit, Oxford University, Dr. Adler is the Clinical Lead for Diabetes at Addenbrooke's Hospital, Cambridge and supervises epidemiology students at Cambridge University.

Setting the Scene; The Burden of Obesity and Metabolic Syndrome; Cardiovascular Risk in Psychiatric Patients



The Implications of Obesity

By Dr Donal O'Shea,
*Consultant Endocrinologist,
 St Vincent's University Hospital,
 Dublin and a member of the Irish Dept
 of Health's National Obesity Taskforce*

Changes in diet, particularly increased portion size, and a decline in exercise have contributed to the well-recognised explosion in obesity of recent years. Dr O'Shea discussed obesity's role in multiple illnesses. Obesity is the cause of 5% of myocardial infarctions; 20% of hypertension; 30% of malignancies; and 80% of type II diabetes mellitus. Non-alcoholic fatty liver is now the commonest cause of referral to a liver clinic. Dr O'Shea suggested that whilst BMI is an imperfect means of measuring body fat, it is effective as a screening tool. It should be noted that appearance is little guide to obesity and one may be quite overweight in BMI terms before any cosmetic problem is noted.

Weight loss is of benefit. A 10% loss in weight leads to a 40% reduction in the chances of developing diabetes mellitus; a 37% reduction in all forms of cancer; a 10 mmHg reduction in blood pressure; and an overall 20% reduction in all-cause mortality.

The treatment of obese patients at Dr O'Shea's clinic was also discussed. This is a difficult to treat group of patients with a 50% failure rate. A multidisciplinary approach is required. Of weight loss medications, only orlistat is regarded as suitable for use in psychiatric patients as the others are associated with mood instability. Gastric reduction surgery has become the commonest elective surgical procedure in the USA. It is used in the Irish context. Some 10% of patients develop new addictions or compulsion patterns after surgery.

Overall, Dr O'Shea emphasised the importance of considering obesity as a factor early in treatment, he advocated the value of screening for it at baseline and of providing appropriate advice, and urged clinicians to consider obesity as a factor when choosing psychotropic medications.

Donal O'Shea qualified from University College Dublin in 1989. He moved to Hammersmith Hospital in London and worked as a registrar in general medicine, cardiology and endocrinology before being appointed as Senior Registrar in the Department of Diabetes & Endocrinology. In 1993 he was awarded a Wellcome Trust Research Training Fellowship and completed the work for an MD thesis entitled The hypothalamic control of appetite and peripheral metabolism. In 1996 he was appointed to the post of Consultant Physician/Senior Lecturer in Diabetes and Endocrinology at Charing Cross Hospital. In 1999 Dr. O'Shea moved to his current position in St Vincent's University Hospital and St Columcille's Hospital Loughlinstown where he currently runs the only hospital based multidisciplinary treatment unit for the management of adult obesity in the country. He was a member of the Department of Health National Obesity Taskforce, chairing the Detection and Treatment subgroup which reported to the Government in May 2005, and has published on diabetes, obesity, steroid metabolism and thyroid disorders.

Managing Cardiovascular Risk in Practice

The importance of cardiovascular risk, and specific issues in psychiatric patients, had been thoroughly discussed. The importance of medication choice had been emphasised. The three final presentations focused most closely on the practical implementation of what had been discussed.



Issues in Managing Organic Disease in Psychiatric Illness

By Prof Kieran Murphy,
*Professor of Psychiatry,
 Royal College of Surgeons in Ireland,
 Beaumont Hospital, Dublin*

The final module of the Masterclass focused on the practical steps that might be taken to implement the advice offered in previous sessions. Professor Murphy began with an historical overview of the development of psychiatry. Aside from its inherent interest, this helped explain a divide between "organic" and "functional" illnesses that continues to be seen and which contributes to psychiatric patients' relatively poor outcome in terms of cardiovascular illness. He discussed the oft-observed pattern whereby general

physicians may see psychiatric illness as the explanation for physical symptoms, often precluding further investigations. Psychiatrists, on the other hand, commonly see physical symptoms as the responsibility of the referring doctor. There are factors particular to psychiatric patients, such as a greater turnover of attending doctors and a tendency not to comply with psychotropic or general medication which further increases this population's risk.

Prof Murphy discussed the evidence base for the various guidelines that have been produced. The recent Wellbeing Support Programme, preliminary results of which are described by Ohlsen et al in the Journal of Psychiatric and Mental Health Nursing, is a nurse led programme which has been implemented in the UK. Registered Mental Health Nurses act as

Managing Cardiovascular Risk in Practice

Nurse Advisors who see new patients for an initial consultation. At this initial consultation blood pressure, glucose, waist circumference, weight and other measures are taken. Advice is given on diet and exercise and referral made to appropriate agencies. Patients are subsequently followed-up at a second consultation where assessments are repeated. It has been found that at the initial consultation 87% of patients are overweight and 60% have an unhealthy diet – and at the second consultation 54% have lost weight and the proportion with an unhealthy diet is reduced to 25%. These are preliminary findings but do demonstrate that relatively modest levels of intervention can have striking results.

CONCLUSIONS

- Physical illness common in patients with mental illness
- Historical issues
- Healthcare system and patient factors act as barriers to recognition and management of physical illness in mentally ill
- Optimum management of patients with mental illness involves integration of physical and mental health needs

Kieran C. Murphy graduated from UCD in 1987 and initially trained in Internal Medicine in the Mater Misericordiae University Hospital, Dublin. He then trained in Psychiatry in St. John of God Hospital, Dublin where he also obtained a Masters Degree in Psychoanalytical Psychotherapy from UCD. He moved to the University of Wales College of Medicine, Cardiff in 1994 where he completed his higher clinical training in Psychiatry and obtained a PhD

in Psychiatric Genetics. In 1999, he was appointed Senior Lecturer in Behavioural Genetics at the Institute of Psychiatry, King's College London and in 2002, took up his current appointment as Professor and Chairman, Department of Psychiatry, Royal College of Surgeons in Ireland. His research interests include the genetics of psychiatric disorders and the assessment and neurobiology of behavioural phenotypes in genetic disorders.



Experiences in Managing Cardiovascular Risk in Psychiatric Patients

By Dr Helen Millar,
*Consultant Psychiatrist,
Carseview Centre, Dundee, Scotland*

As had been extensively discussed at the Masterclass, not only were cardiovascular risk factors more prominent in psychiatric patients but multiple factors were also evident. In Dundee, Dr Millar and her team adopted a holistic approach to this issue. They set up a Health Screen Clinic as part of their service. This was based on the principles that the mentally ill are as entitled to health screening as the general

population, that psychiatric services play a vital role in the physical health of patients, and that physical well being is closely related to mental well being.

The Health Screen Clinic aimed to be a “one-stop shop” for physical and mental health. It was also intended to act as a form of triage for primary care. Begun in 2002, it included all from 16 to 65 who agreed to attend who were on antipsychotic medication. As routine screening, FBC, U&Es, LFTs, Thyroid Function, Prolactin, Total cholesterol and random blood glucose levels were performed. Blood pressure, pulse, BMI calculations, and a full history of family illnesses and lifestyle were performed. The clinic also used the Drug Attitude Inventory and the Liverpool University Side-Effect Rating Scale to assess compliance issues and presence or absence of drug side effects. 72% of the patients had a diagnosis of schizophrenia, 7% had a diagnosis of schizoaffective disorder, 12% had a diagnosis of bipolar disorder and 9% had a diagnosis of depression. 20% were on two antipsychotic while 25% were on clozapine.

The clinic has had much success in engaging patients and has a high uptake of participation in the various teams and sports offered.

Dr Millar also explored how a focus on general health was not seen as threatening by the patient population. Quite the contrary; it provided an alternative and perhaps less threatening focus to engage patients and proved in many ways clinically useful from a purely psychiatric point of view.

Helen Millar is a consultant psychiatrist, trained in both General Adult and Forensic Psychiatry across Scotland, Northern Ireland and England. Forensic settings included HMP Maze, The Raeside Clinic and The State Hospital, Carstairs.

She is currently the Lead Clinician of a Community Mental Health Team in Dundee covering a deprived catchment area of 45,000 patients and is the Lead Clinician of a 12 bedded male Intensive Psychiatric Care Unit in the Carseview Centre, Dundee.

She has an active interest in clinically based research and most recently been involved in developing and piloting an innovative web based integrated electronic record system for the Tayside psychiatric population. She is also actively involved in clinical trial work, particularly looking at effectiveness of new antipsychotic medication.



Models of Implementation of managing Cardiovascular Risk in Psychiatric Patients

By Prof Kevin Malone,
*Professor of Psychiatry,
St Vincent's University Hospital*

Professor Malone discussed the models for implementation of the clinic models discussed. He examined the existing service interfaces for those with mental illness, and in particular how these

Managing Cardiovascular Risk in Practice

related specifically to management of cardiovascular risk. He discussed the mainstays of intervention from a psychiatrist's point of view, such as minimisation of polypharmacy and the use of alternative pharmacotherapy. Four models of care were outlined including:

- Psychiatrist to provide combined psychiatric and CVD care;
- Joint psychiatry/CVD Clinic care;
- Screening and transferring risk patients to Metabolic care; and
- Primary care and public health model.

Professor Malone also discussed the "Super-12" approach used in St Vincent's Hospital for patients with super-obesity, serious psychiatric illness and cardiovascular morbidity. One patient a month each year is admitted under the team relevant to the immediate presenting problem. Intensive multidisciplinary work follows. Early results suggest this approach lead to significant and sustained weight loss illustrating a promising interdisciplinary clinical strategy.

Kevin Malone was appointed to the Chair of Psychiatry at St. Vincent's University Hospital, University College Dublin in September 2002. He graduated in medicine from the Royal College of Surgeons in 1984. In 1991, he was awarded a two-year International Fogarty Research Fellowship by National Institutes of Health (USA) to conduct Neurobiology Studies on Suicidal Depression at the University of Pittsburgh, and was awarded an M.D. degree for his research in 1994. In 1994 he moved to the Dept. of Neuroscience, College of Physicians and Surgeons of Columbia New York, where he was appointed Associate Professor of Psychiatry and Director of Clinical Evaluation and Treatment Studies

at the Columbia University Center for Suicide Research. He returned to Ireland in 1998 to take up the post of Consultant Psychiatrist / Senior Lecturer at the Dept. of Adult Psychiatry, Mater Hospital / UCD. He was appointed Professor of Psychiatry at St. Vincent's University Hospital and University College Dublin in 2002.

Amongst his awards, he received a Distinguished Investigator Award from the American Foundation for Suicide Prevention for his brain imaging studies of suicidal depression. He was awarded Membership of the Royal College of Physicians in Ireland in 2001, based on his published work, and awarded Fellowship of The Royal College in 2004.

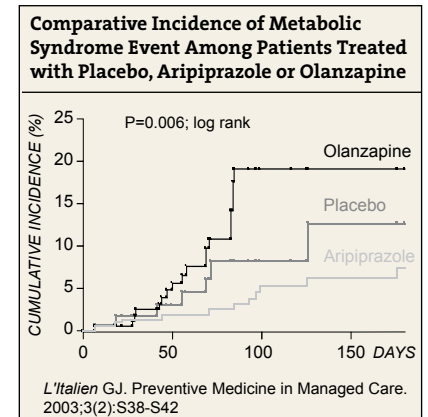
Cardiovascular Risk Specific to Psychiatric illness and antipsychotic medication

Praising the holistic focus of the meeting in terms of bringing cardiologists, endocrinologists and psychiatrists together, Dr Sean Dinneen said during his presentation that clinicians such as he regularly saw a form of diabetes amongst schizophrenia patients that he didn't believe was fully understood. *It is incumbent on psychiatrists and endocrinologists to co-operate in achieving the best possible treatment for this group.* As well as the setting out the stark facts regarding the effects on general health of obesity, hypertension and type II diabetes, all speakers agreed that there were specific issues regarding psychiatric patients.

A substantial proportion of the excess risk of metabolic abnormalities in patients with psychiatric disease may be attributed to lifestyle factors. These were discussed by many speakers. Dr Emer Shelley of the Department of Health and Children described the decreasing mortality rates from cardiovascular diseases in Ireland, especially from coronary heart disease and stroke. These trends are similar to those in other Western societies. Alongside this, and largely because of improvements in survival, there has been an increase in the prevalence of these conditions. Discharges from acute hospitals for coronary heart disease and heart failure have increased. The prevalence of type II diabetes mellitus is increasing, as a result of increased body mass index and physical inactivity. Crucially, the changes associated with the decline in cardiovascular mortality (smoking, diet and improvements in blood pressure and cholesterol levels) are greater in higher socioeconomic groups. Lower socioeconomic groups have fared less well. The gap in health experience has widened between the better off and vulnerable groups in society, such as psychiatric patients.

Medication is an important factor in determining cardiovascular risk in psychiatric patients. Dr Brendan Buckley, in his presentation, addressed the role of antipsychotics in dyslipidaemia. He

draw attention to substantial differences between the effects of different antipsychotic drugs on plasma lipid profile and he advocated that doctors should be more selective in their use of antipsychotic drugs to avoid increasing cardiovascular risk. He instanced a number of studies which showed that olanzapine, in general, significantly increased LDL while the lipid effects of risperidone were neutral and those of olanzapine and ziprasidone were potentially beneficial to cardiac risk. He warned that both epidemiological and intervention studies uniformly suggested that a 1% increase in circulating LDL cholesterol causes a 2% increase in cardiac risk.



Cardiovascular Risk Specific to Psychiatric illness and antipsychotic medication

The endocrinologist urged psychiatrists to look for dyslipidaemia in psychiatric patients and to actively treat it. In response to a question from the floor after his talk, Dr Buckley advised that, where significant lipid disorder was present, it was more appropriate to change antipsychotic drug if possible a more 'lipid-benign' alternative. However, addition of statin therapy is appropriate when this is not possible, Dr Buckley added.

Professor Ted Dinan explored the relationship between antipsychotic medication and weight gain. Some newer antipsychotics have more of an effect on weight and other parameters than others. "Anti-psychotics in general, but atypical anti-psychotics in particular, can produce metabolic disturbance that will impact on the risk of cardiovascular disease in psychiatric patients. There is a hierarchy in terms of impact and clinicians should be aware of it," said Professor Dinan.

Detailing this hierarchy of metabolic impact, the psychiatrist said clozapine was particularly problematic in that it had the most severe effect. It was followed by olanzapine, which shared a similar structure to clozapine. Next in the metabolic league table were phenothiazines followed by butyrophenones and risperidone, the latter two being about equal. Aripiprazole has the lowest propensity for metabolic disturbance.

THE HIERARCHY OF METABOLIC IMPACT AMONG ANTIPSYCHOTIC MEDICATIONS

Rank	
1	Clozapine
2	Olanzapine
3	Phenothiazine
4	Butyrophenones Risperidone
6	Aripiprazole

Source: Dinan, RCPI Masterclass, 2/12/05

Attendees at the Masterclass asked about early weight gain on olanzapine. Professor Dinan replied that this side effect was particularly prominent at the onset of treatment, particularly in the first twelve weeks when close monitoring was required. He added that weight gain can continue after this in some instances and must be constantly kept in mind.

Dr Donal O'Shea also reinforced the message on the importance of obesity in general, and medication choice bearing obesity in mind in particular. Obesity of itself is of relevance in psychiatric practice. In the United States, it has been found that obese female adolescents are more likely to live in poverty, to be less educated, and to earn less as their non-obese peers. White American women who are depressed and obese are more likely to be suicidal. Interestingly, this does not apply to black women. Even before starting medication, 18-25% of psychiatric patients are obese and 2-5% have Grade Three obesity. Most weight gain associated with antipsychotics occurs in the first year, and is primarily visceral fat. Dr O'Shea reiterated that clozapine and olanzapine are most associated with weight gain while aripiprazole and ziprasidone are least associated.



Are Patients with Psychosis Predisposed to Metabolic Abnormalities?

By Dr Jogin Thakore,
Consultant Psychiatrist,
St Vincent's Hospital, Fairview, Dublin

Dr Thakore began with an overview of the issue. He discussed the possibility that surveillance bias might account for the greater incidence of metabolic syndrome in patients on atypical antipsychotics. Patients prescribed atypicals were 40% more likely to be tested. Leslie et al's work on predicting time to diabetes mellitus in outpatients with schizophrenia on monotherapy of first or second generation antipsychotics, found that the attributable risk associated with these medications was highest for clozapine (2.03%), followed by quetiapine (0.80%), olanzapine (0.63%), and risperidone (0.05%)

This implies that the illness of schizophrenia may be associated with visceral obesity itself which plays a role in the development of type II diabetes mellitus. 15.4% of non-obese drug naïve first episode patients with schizophrenia, in Dr Thakore's studies,

have impaired fasting glucose and are insulin resistant. There is a family history of diabetes mellitus in 19-30% of patients with schizophrenia, well above the population average. Dr Thakore concluded that the precise magnitude of the role of antipsychotics in the metabolic abnormalities seen in patients with schizophrenia is still to be elucidated. Family members of schizophrenia sufferers form a group suitable for screening for type II diabetes mellitus.

Jogin H. Thakore, MB, PhD, MRCPsych, is a Clinical Psychiatrist at the Neuroscience Centre of St. Vincent's Hospital, Fairview in Dublin, Ireland, and Senior Lecturer in Psychiatry in the Department of Psychiatry at the Royal College of Surgeons in Ireland. Having graduated from Trinity College Dublin, he went on to train first in Ireland and then in London early in his career, where he obtained his MRCPsych and PhD in Psychiatry at the University of London. Upon returning to Ireland, he was awarded the MRCPsych.

Dr. Thakore's principal area of research is cardiovascular risk factors in schizophrenia and basic sensory processing deficits in schizophrenia and subjects at high risk for schizophrenia. The evoked related potential studies are in collaboration with John Foxe at the Nathan Kline Institute for Psychiatric Research in New York, and Ian Robertson at TCD.

Cardiovascular Risk Specific to Psychiatric illness and antipsychotic medication



Metabolic Burden in Patients with Schizophrenia

By Dr Marc de Hert,
Clinical Psychiatrist
University Centre St Jozef, Katholieke
Universiteit Leuven, Belgium

Dr de Hert discussed the UC Metabolic Studies which his centre in Belgium have carried out. Firstly he gave an overview of the relationship between schizophrenia and metabolic risk factors.

Of the 200 non diabetic schizophrenic patients who were recruited into the trial, 25.5% had glucose abnormalities at baseline. It was noticeable that cessation of medication - due to poor patient compliance - was associated with a reversal of the metabolic changes. Indeed, Dr de Hert observed that the development of some metabolic effects could almost be seen as a proxy marker for compliance. 25% required treatment with statins.

The Second UC Metabolic Study focused on first treatments for psychosis. Weight gain was observed on all products, most notably on olanzapine. Of these patients, 15.4% met criteria for statin use at three months. Aripiprazole not only had less of a

cholesterol-raising effect, it acted as a lipid stabiliser with a lipid-lowering effect 50% of that of a potent statin.

Dr de Hert discussed the American Psychiatric Association's recommendations for monitoring of cardiovascular risk factors for patients on antipsychotics. He argued that the APA's recommendation - baseline fasting lipids, repeated at five years - leaves far too long between tests as the effect on lipids can be seen after weeks and months.

In response to questions from the floor, Dr de Hert reported that contrary to many people's expectations, psychotic patients had proven to be quite amenable to being informed of the potential cardiovascular risks they face and the rationale for the study.

Marc De Hert, MD, PhD, is a clinical psychiatrist and psychotherapist and Head of Ward Treatment of Psychosis at University Centre St. Jozef (Catholic University Louvain), Kortenberg, Belgium. He has a PhD in suicide in young schizophrenic patients and was appointed the Medical Director of Brussels Night Hospital in Brussels. His major research interests in psychosis and schizophrenia are health economics, family burden, rehabilitation, epidemiology, outcome research, and metabolic aspects of antipsychotic medication.



Antipsychotic Agents - Mechanism of Metabolic Disorders

By Dr Marilyn Ader,
Associate Professor, Dept of Physiology
& Biophysics, University of Southern
California, Los Angeles, California, USA

Dr Ader reviewed the physiology of glucose homeostasis and the possible mechanisms by which antipsychotics may cause metabolic dysfunction and overt diabetes. Antipsychotics have been associated with the development of obesity, as well as insulin resistance, impaired pancreatic beta cell function, and diabetic ketoacidosis. While insulin resistance greatly increases risk of developing type II diabetes, resistance alone is insufficient to result in diabetes. To explain this, Dr Ader introduced the concept of the disposition index - the product of insulin sensitivity and insulin secretion, which reflects the ability of the pancreas to upregulate secretion when insulin resistance develops. In most cases - the particular example given was of a pregnant woman - secretion increases when insulin sensitivity declines in normal pregnancy, and these processes re-

regulate after delivery, thus maintaining glucose tolerance. The inability of beta cells to compensate for insulin resistance is the critical defect in the pathogenesis of type II diabetes.

From clinical reports, it is clear that many atypical antipsychotics cause weight gain, although the magnitude varies amongst agents. Glucose intolerance and insulin resistance may develop during atypical antipsychotic use, although the extent and clinical relevance of these changes remain unclear in the absence of well-controlled prospective studies of metabolic function in the treated psychiatric population.

Dr Ader described animal studies intended to ascertain the extent to which atypical antipsychotics cause metabolic dysfunction in the absence of psychiatric disease. These studies were performed in dogs, studied before and after 6 weeks of drug treatment. Adiposity was measured via abdominal MRI, insulin sensitivity was measured by hyperinsulinaemic clamp, and insulin secretion was measured by hyperglycaemic clamp. These studies demonstrated marked metabolic changes with olanzapine versus risperidone. With the former, there was profoundly increased adiposity, severe hepatic insulin resistance, and complete blockade of beta cell compensation for resistance. The metabolic changes were independent of drug-induced changes in body weight or adiposity, as placebo-treated dogs exhibited comparable weight gain, but no pronounced metabolic abnormalities.

In clinical studies in subjects with schizophrenia, it was found that both olanzapine (by six weeks) and risperidone (by twenty four weeks) induced adiposity as assessed by DEXA and CT scan. In African American and Hispanic subjects, olanzapine induced dysfunction in beta cell compensation by week 24.

Cardiovascular Risk Specific to Psychiatric illness and antipsychotic medication

Marilyn Ader is Associate Professor in the Department of Physiology and Biophysics at the Keck School of Medicine of the University of Southern California (USC) in Los Angeles. Dr. Ader received her B.S. degree in Biology from Utica College of Syracuse University, and her M.S. degree from Kent State University. She was awarded her Ph.D. in Physiology and Biophysics from USC in 1988 for groundbreaking work on mechanisms of insulin action to regulate glucose production. Her major research interests are the regulation of glucose tolerance, insulin resistance, and insulin secretory function and the mechanisms by which obesity increases risk for Type II diabetes.



Does Current Management Exacerbate Risk?

Dr Brian O'Shea,
Consultant Psychiatrist, Newcastle Hospital, Greystones, Co Wicklow

Dr O'Shea offered a comprehensive overview of the history of psychiatric illness and the cardiovascular risk associated with treatments offered to address the condition.

He concluded by highlighting the results of an audit of the Cardea Cardiovascular Risk Factor Assessment Programme, a retrospective audit of services that involved a number of urban and rural community services.

The research strongly supports the need to carry out cardiovascular risk assessment in psychiatric patients.

Key findings from the 709 patients involved in the programme included:

- The detection of 11 new cases of diabetes mellitus
- On presentation, 86% of patients had either no recorded history or unknown history of hypertension. 6% of these patients had a systolic blood pressure above 140
- 30.1% of patients with no recorded history of cardiovascular disease were in fact at high risk of cardiovascular death
- Of the patients at high risk, only 0.6% were on an anti-platelet agent or diuretic, 3.1% were on a statin, and none were on an ACE-inhibitor or a beta-blocker

Brian O'Shea FRCPsych qualified in Medicine from University College Dublin in 1974. He trained in psychiatry in Dublin and was a Consultant Psychiatrist in St. Brendan's Hospital for two years before moving to Newcastle Hospital, Co. Wicklow in 1985 where he is Clinical Director. He has published many papers on such subjects as phenomenology, malignancy in relation to psychiatry, factitious disorders, electroconvulsive therapy, neuropsychiatry, pharmacotherapy, dynamic psychotherapy, self-help organisations, and the history of psychiatry. His books include a textbook of psychological medicine (4 editions), advances in schizophrenia research (2 volumes), and essays in psychiatry (2 volumes). He is an experienced examiner in both parts of the MRCPsych.

Masterclass Workshop – Models of Implementation of Managing Cardiovascular Risk in Psychiatric Patients

K. Malone, D. O'Shea, B. Maurer, J Feely, B. Buckley and TJ McKenna

Workshop Report: After the main presentations, the Masterclass split into workshops to discuss the models of implementation of managing cardiovascular risk in psychiatric patients.



Aim: To explore and elucidate the clinical burden-of-care of metabolic syndrome and cardiovascular risk in patients with major psychiatric illness with a view to proposing best-fit models of care.

Methods: A European symposium was convened at The Royal College of Physicians in Ireland comprising representation from psychiatry cardiology, endocrinology and primary care from 10 European countries to explore the clinical consequences of metabolic syndrome and cardiovascular risk in patients with psychiatric illness. An end-of-symposium workshop was convened to ascertain the views of many of these clinicians, and existing best-practice models of care were outlined and synthesized.

Results: Across a range of international settings, patients with major psychiatric illness are disadvantaged from seeking clinical medical care by the very nature of their illness. Few practical clinical models of care exist internationally. This

may relate to limited financial resources currently available for medical care to psychiatric patients with co-existing metabolic and cardiac problems which are at times iatrogenically induced. Four models of care were proposed (a) Psychiatrist to provide combined psychiatric and CVD care; (b) joint psychiatry/CVD Clinic care; (c) screening and transferring risk patients to Metabolic care; and (d) primary care and public health model. No single model satisfied all clinician groups, with each model having strengths and weaknesses depending on a variety of demographic, clinical expertise and financial resource factors.

Conclusions: A significant gap in clinical research knowledge and clinical care has been identified with regard to specific and at times iatrogenic medical needs of patients with major psychiatric illness, contributing to increased morbidity and mortality in this patient group. Best-fit, patient-centred models of care need to be designed and rigorously evaluated.

Speakers' details

Hearts & Minds: Exploring the cardiovascular risk burden in psychiatric disease

Dr Marilyn Ader

Associate Professor, Dept of Physiology & Biophysics, University of Southern California, Los Angeles, California, USA

Dr Amanda Adler

Consultant Physician, Addenbrookes Hospital, Cambridge, England, UK

Dr Brendan Buckley

Consultant Endocrinologist, University College Cork

Prof Ted Dinan

Professor of Psychiatry, Cork University Hospital

Dr Sean Dinneen

Consultant Endocrinologist, University College Hospital, Galway

Prof John Feely

Professor of Pharmacology & Therapeutics, Trinity College Dublin; Consultant Physician, St. James's Hospital, Dublin

Dr Marc de Hert

Clinical Psychiatrist, University Centre St Jozef, Katholieke Universiteit Leuven, Belgium

Dr Vincent Maher

Consultant Cardiologist, Adelaide & Meath Hospital, Dublin

Dr Colm McDonald

Professor of Psychiatry, National University of Ireland, Galway

Prof Kevin Malone

Professor of Psychiatry, St Vincent's University Hospital, Dublin

Dr Brian Maurer

Consultant Cardiologist, St. Vincent's University Hospital, Dublin

Dr Helen Millar

Consultant Psychiatrist, Carseview Centre, Dundee, Scotland, UK

Prof Kieran Murphy

Professor of Psychiatry, Royal College of Surgeons in Ireland, Beaumont Hospital, Dublin

Dr Brian O'Shea

Consultant Psychiatrist, Newcastle Hospital, Greystones, Co Wicklow

Dr Donal O'Shea

Consultant Endocrinologist, St Vincent's University Hospital, Dublin

Dr John Sheehan

Consultant, Liaison Psychiatry, Mater Misericordiae University Hospital & Rotunda Hospital, Dublin

Dr Emer Shelley

National Heart Health Advisor, Dept of Health & Children, Dublin

Dr Seamus Sreenan

Consultant, Diabetes & Endocrinology Dept, Connolly Hospital, Blanchardstown, Dublin

Dr Jogin Thakore

Consultant Psychiatrist, St Vincent's Hospital, Fairview, Dublin

