Institution: King's College London

Unit of Assessment: UoA5

Title of case study: Reducing Harmful Use of Antipsychotics in People with Dementia

1. Summary of the impact: King's College London researchers have had a major widespread impact on medical care for people with dementia. They have demonstrated the limited benefit and considerable harm done by the use of antipsychotics in dementia patients. Their follow-on campaigning and policy work brought this major health issue to the forefront of the political agenda and led them to work with the Department of Health to create a best practice guide, now widely used nationally and internationally. In addition, they have worked with the BMJ to develop an e-learning package for General Practitioners. The combined impact of this work has made a major contribution to a 60% reduction in the use of antipsychotic drugs in people with dementia in the UK and major changes in practice internationally, preventing 1000's of unnecessary deaths.

2. Underpinning research: In the UK there are around 800,000 people with dementia. Up to 90% of these individuals will experience behavioural and psychological symptoms (BPSD) such as aggression, agitation and psychosis with huge personal cost to the patient and their carers. Work at King's College London (KCL) on treatment for BPSD has been carried out by Prof Clive Ballard (2003-present, Professor of Age Related Diseases), Prof Robert Howard (1998-present, Professor of Old Age Psychiatry) and Prof Sube Banerjee (1992 -2012, Professor of Mental Health and Ageing).

In the mid 2000's it was estimated that up to 25% of people with dementia, and more than 45% of those with dementia living in care homes, were being prescribed antipsychotics for BPSD. However, KCL researchers questioned both the efficacy and safety of such medications in these patients. One KCL-led randomised, controlled trial (RCT) involving 93 patients (in collaboration with colleagues at Oxford and Newcastle Universities) demonstrated that the atypical antipsychotic (AA) quetiapine was ineffective in the treatment of aggression and psychosis in people with Alzheimer's disease (1). A KCL led meta-analysis showed that many other AAs, including risperidone, olanzapine and aripiprazole, conferred only very modest benefits (2). The DART-AD trial was a KCL-led RCT involved dementia patients continuing typical or atypical antipsychotic treatment (n = 51) or switching to a placebo (n = 51). For most, there was no overall detrimental effect on BPSD and some benefits were seen in functional and cognitive status over 6-12 months following antipsychotic withdrawal (3). Of particular importance, there was, however, a significantly increased long term risk of mortality for patients continuing antipsychotic treatment versus those on placebo. Cumulative survival at 24 months was 46% vs 71%; at 36-months it was 30% vs 59% (4). Overall, these studies highlighted significant associations between AAs and greater cognitive decline, stroke and a very substantial and accumulating increase in mortality over time.

A key barrier for clinicians discontinuing or withholding antipsychotic drugs is the fear that BPSD cannot be effectively treated with alternative approaches. The DART-AD trial (3,4) demonstrated that antipsychotics can be withdrawn without significant worsening of BPSD and following on from this, KCL led a trial of person-centred care training for staff in 12 care homes (focused intervention training and support: FITS). Over 9 months, antipsychotic use was reduced by 50% in the intervention care homes but was unchanged in the facilities not receiving the FITS intervention, without any worsening of BPSD (5). KCL work including clinical trials and meta-analyses have also highlighted the limited utility of anti-dementia drugs and anticonvulsants in treating BPSD (6, 7) but highlighted the potential value of the anti-depressant mirtrazapine as a therapy for agitation (8). The development of evidence to support alternative treatment approaches and to highlight pharmacological treatments that are not efficacious has contributed to enabling the reduction in antipsychotic drugs to be achieved without a major increase in the prescription of alternative non-evidence based pharmacological therapies.

3. References to the research

1. Ballard C et al Quetiapine and rivastigmine and cognitive decline in Alzheimer's disease: randomised double blind placebo controlled trial. BMJ 2005;330(7496):874. Doi: 10.1136/bmj.38369.459988.8F (145 Scopus citations)
2. Ballard C, Howard H. Neuroleptic drugs in dementia: benefits and harm. Nat Rev Neurosci 2006; 7(6):492-500. Doi: 10.1038/nrn1926 (83 Scopus citations)
3. Ballard C, et al Investigators DART AD. A randomised, blinded, placebo-controlled trial in dementia patients continuing or stopping neuroleptics (the DART-AD trial). PLoS Med

2008;5(4):e76. Doi: 10.1371/journal.pmed.0050076 (70 Scopus citations)
4. Ballard C, et al DART-AD investigators. The dementia antipsychotic withdrawal trial (DART-AD): long-term follow-up of a randomised placebo-controlled trial. Lancet Neurology 2009a;8(2):151-57. Doi: 10.1016/S1474-4422(08)70295-3 (184 Scopus citations)
5. Fossey J, et al (Howard R senior author). Effect of enhanced psychosocial care on antipsychotic use in nursing home residents with severe dementia: cluster randomised trial. BMJ 2006;332(7544):756-61 (154 Scopus citations)
6. Howard RJ, et al. Donepezil for the treatment of agitation in Alzheimer's Disease. NEJM 2007; 357:1382-92. Doi: 10.1056/NEJMoa066583 (119 Scopus citations)
7. Ballard CG, et al. Management of agitation and aggression associated with Alzheimer disease. Nature Reviews Neurosci 2009; 5:245-55. Doi: 10.1038/nrneurol.2009.39 (85 Scopus citations)
8. Banerjee S, et al. Sertraline or mirtazapine for depression in dementia (HTA-SADD): a randomised, multicentre, double-blind, placebo-controlled trial. Lancet 2011; 378(9789):403-11. Doi: 10.1016/S0140-6736(11)60830-1 (75 Scopus citations)

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4. Details of the impact

KCL research guides government policy: In the late 2000's, a number of government documents arose highlighting the issues surrounding the prescription of antipsychotic medication to people with dementia. A report on improving services for people with dementia from the House of Commons Public Accounts Committee, to which Prof Banerjee gave evidence, specifically discussed the work of KCL when questioning antipsychotic prescribing practices (1a). This report is cited in the Department of Health's (DoH) consultation on the National Dementia Strategy, which, mirroring conclusions of KCL research, posits that two ways care for residents in care homes could be improved is by "*deployment of non-pharmacological management strategies for behavioural disorders in dementia*" and by "*specialist input into decision making concerning the initiation, review and cessation of antipsychotic medication for people with dementia*" (1b). Prof Clive Ballard was a key advisor for reports published in 2008 by Paul Burstow, MP and the All Party Parliamentary Group on Dementia. Burstow uses the findings of Fossey 2006 to support that "*promotion of person-centred care...in the management of patients with dementia with behavioural symptoms provides an effective alternative to antipsychotic drugs*" (1c). The latter, an enquiry into the use of antipsychotic drugs in people with dementia in care homes, also uses Fossey to say that "*training and support for care home staff reduces the need to use antipsychotics in residents with dementia and can be a viable alternative for managing challenging behaviour*" (1d).

Following these, in 2009, the DoH produced a report led by Prof Banerjee that details how unnecessary antipsychotic prescribing in people with dementia in the UK is estimated to lead to 1800 deaths and 1600 cerebrovascular adverse events every year (2e). The report cites a number of KCL led studies including Fossey 2006 when discussing prevalence of antipsychotic prescribing in nursing homes and how behavioural interventions can help reduce the need for antipsychotics. For instance, when stating that "*there is a clear emerging consensus about the positive and negative effects of antipsychotic drugs*," the report cites Ballard 2006 and a 2009 review by Prof Ballard containing this paper, along with Ballard 2005, 2009a and 2009b (2f). It also cites the DART-AD trial (Ballard 2008, 2009b) when saying how "*continuation compared with cessation of antipsychotic medication was associated with increased mortality*." The government response to this report included that it needed to "*ensure that antipsychotic drugs are only prescribed to people with dementia when necessary and are not used when non-pharmaceutical approaches can be equally effective*" (2g).

KCL research guides practice: This body of policy work led to the development of the 2011 Best Practice Guide on optimising treatment and care for BPSD, written by KCL researchers in partnership with the DoH and supported by the Dementia Alliance, provides clear guidance on appropriate use of antipsychotics and safer alternatives. It also provides a toolkit following a basic stepped care model and includes clinical checklists and guidance on symptom assessment, treatment and monitoring. It cites Ballard 2008 and 2009b as two of only 10 key references and Ballard's 2009 paper (1f) as a key review (2a). The guide has been accessed online more than

100,000 times and been distributed to over 15,000 UK clinicians. It is available in six languages, with wide international dissemination. In parallel, KCL, the Alzheimer's Society and the BMJ developed an e-learning package for GPs (2b). The guide is referenced in many government websites such as the NHS's Clinical Knowledge Summary on Dementia (that also cites Ballard 2005) (2c) and is as a key resource in the DoH's Dementia Commissioning Pack (2d).

Current National Institute for Health and Care Excellence (NICE) guidelines on 'Supporting people with dementia and their carers' state that "*people with...dementias with mild-to-moderate non-cognitive symptoms should not be prescribed antipsychotic drugs because of the possible increased risk of cerebrovascular adverse events and death*." They back this with studies including Ballard 2005 and they use Fossey 2006 when discussing the utility of training and support when aiming to reduce drug use and agitation in nursing homes (2e). Banerjee's 2009 report is also cited in the 2010 NICE 'Dementia quality standard' discussing challenging behaviour (2f).

Regulatory Impact: KCL research has also contributed to two Medicines and Healthcare products Regulatory Agency's (MHRA) working groups in 2009 (3a, with Ballard 2009a as a resource) and 2012 (3b, citing Ballard 2006 and Banerjee's report). These highlight the increased risk of stroke and death with antipsychotics in people with dementia and led to warning letters circulated to all doctors in the UK. The MHRA also produced an 'Antipsychotics Learning Module' that cites NICE guidance and Prof Banerjee's 2009 report (3c).

Overall Impact in Reducing Antipsychotic use in people with dementia: The combination of these efforts has led to a massive reduction in antipsychotic prescribing to people with dementia. Part of the government response to Prof Banerjee's report on antipsychotic prescribing was to appoint a National Clinical Director for Dementia. One of their responsibilities was to provide the 2012 NHS audit of English primary care GP practices that encompassed almost 200,000 people with dementia. This showed a 60% reduction in antipsychotic use from 2006 to 2011 (4a). With permission from KCL, the FITS intervention is being implemented by the Alzheimer's Society, the DoH, the University of Worcester and HC-One care homes into a person-centred care training package that is being trialled in 150 UK care homes, involving more than 5,000 people (4b).

KCL research making an impact across the globe and raising public awareness: KCL researchers serve as members of the US Alzheimer's Association and Ballard's 2009 review (1f) is cited in their report 'Challenging Behaviors' (5a). They have also worked with the US nursing home regulator Centers for Medicare & Medicaid Services, who in 2012 launched a national initiative to improve behavioural health and minimise medication use in people with dementia (5b). The 'Time for action' report is also cited in the WHO 'Dementia: a public health priority,' jointly developed with Alzheimer's Disease International, when highlighting issues in the use of antipsychotic medication for people with dementia (5c). The contribution of KCL to raise public awareness includes extensive communication through the lay media, including over 250 national television and radio interviews and a key role in developing a 2010 BBC1 Panorama episode addressing antipsychotic use in people with dementia (5d). They are also involved in development of information packages to empower carers of people with dementia to have more informed discussions regarding prescribing decisions, such as those produced by the Alzheimer's Society (5e).

5. Sources to corroborate the impact

1. KCL research guides government policy

a. House of Commons Committee of Public Accounts. Improving services and support for people with dementia. 2008. (pg 34, Ev14). http://www.publications.parliament.uk/pa/cm200708/cmselect/cmpubacc/228/228.pdf
b. DoH. Transforming the quality of dementia care: consultation on a national dementia strategy. 2008(pgs47/48):http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_085567.pdf
c. Paul Burstow MP: Keep Taking the Medicine 4. 2008. paulburstow.org.uk/en/document/keep-taking-the-medicine-4.pdf
d. All-Party Parliamentary Group on Dementia: 'Always a Last Resort.' April 2008. http://www.alzheimers.org.uk/site/scripts/download_info.php?fileID=322
e. The use of antipsychotic medication for people with dementia: Time for action. Nov 2009. http://www.rcpsych.ac.uk/pdf/Antipsychotic%20Bannerjee%20Report.pdf
f. Ballard CG, et al. Management of agitation and aggression associated with Alzheimer disease.

Nat Rev Neurol 2009;5(5):245-55. Doi: 10.1038/nrneurol.2009.39
g. Government response to Professor Sube Banerjee's Report on the prescribing of anti-psychotic drugstopeoplewithdementia:12Nov2009:http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_108363.pdf

2. KCL research guides practice

a. Alzheimer's Society/Department of Health (UK): Optimising treatment and care for behavioural and psychological symptoms of dementia. A best practice guide for health and social care practitioners. 2011. http://www.alzheimers.org.uk/site/scripts/download_info.php?fileID=1163; References: http://www.alzheimers.org.uk/site/scripts/documents_info.php?documentID=1675
b. BMJ Learning. Management of dementia in primary care. March 2012. http://learning.bmj.com/learning/module-intro/dementia-primary-care.html?moduleId=10032231&searchTerm="dementia"&page=1&locale=en_GB
c. NHS's Clinical Knowledge Summary: Dementia. May 2012 http://www.cks.nhs.uk/dementia/management/scenario_ongoing_management#-406488
d. Commissioning Pack resources: Reduce inappropriate prescribing of antipsychotics: http://webarchive.nationalarchives.gov.uk/20130107105354/http://dementia.dh.gov.uk/dementia-commissioning-pack/commissioning-pack-resources-antipsychotics/
e. NICE-SCIE guideline on supporting people with dementia and their carers in health and social care: http://www.nice.org.uk/nicemedia/live/10998/30320/30320.pdf
f. NICE Dementia quality standard QS1. June 2010. Non-cognitive symptoms and behaviour that challenges. http://publications.nice.org.uk/dementia-quality-standard-qs1/quality-statement-7-non-cognitive-symptoms-and-behaviour-that-challenges

3. Regulatory Impact

a. Antipsychotic use in elderly people with dementia. Drug Safety Update March 2009, vol 1 issue 8: http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON088116
b. Antipsychotics: initiative to reduce prescribing to people with dementia. Drug Safety update May2012,5(10):http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON152729
c. MHRA: Antipsychotics Learning Module. 2009. http://www.mhra.gov.uk/ConferencesLearningCentre/LearningCentre/Medicineslearningmodules/Antipsychoticslearningmodule/CON155606?useSecondary=&showpage=33

4. Overall Impact in Reducing Antipsychotic use in people with dementia

a. Focused Intervention Training and Support (FITS): http://alzheimers.org.uk/FITS
b. National Dementia & Antipsychotic Prescribing Audit 2012. Clinical Audit Support Unit: https://catalogue.ic.nhs.uk/publications/clinical/dementia/nati-deme-anti-pres-audi-summ-rep/nati-deme-anti-pres-audi-summ-rep.pdf

5. KCL research making an impact across the globe and raising public awareness

a. Alzheimer's Association – Challenging Behaviors.http://www.alz.org/documents_custom/statements/challenging_behaviors.pdf
b. Centers for Medicare & Medicaid Services website: http://www.nhqualitycampaign.org/star_index.aspx?controls=dementiaCare; resource by Prof Ballard: http://www.nhqualitycampaign.org/files/CliveBallardPresentation.pdf
c. World Health Organisation: 'Dementia: a public health priority.' 2012: http://whqlibdoc.who.int/publications/2012/9789241564458_eng.pdf
d. BBC TV Panorama. What Have the Drugs Done to Dad? Aired 1.11.2010. http://www.bbc.co.uk/programmes/b00vz22h
e. Alzheimer's Society 2011. Reducing the use of antipsychotic drugs: http://www.alzheimers.org.uk/site/scripts/download_info.php?fileID=1133