

# Update on the evidence to support deprescribing

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# To cover the following

- Evidence that it isn't harmful....
- Evidence that it does some good.....
- Controversial areas
  - Bisphosphonates
  - PPIs
  - Anti-diabetes medicines
- STOPPFrail recommendations
- Economics of deprescribing

# Evidence that it isn't harmful

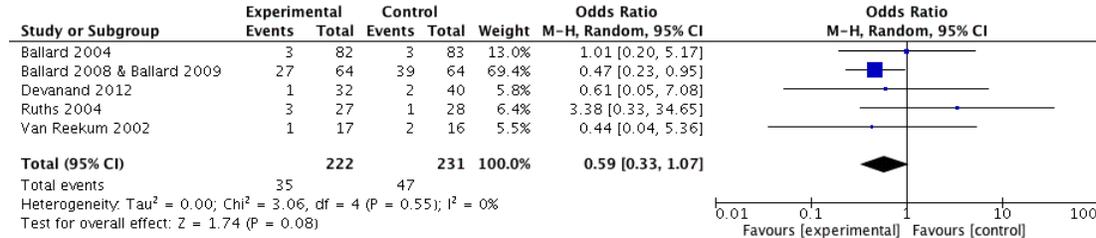
The feasibility and effect of deprescribing in older adults on mortality and health: a systematic review and meta-analysis.

Br J Clin Pharmacol. 2016; 82: 583 – 623

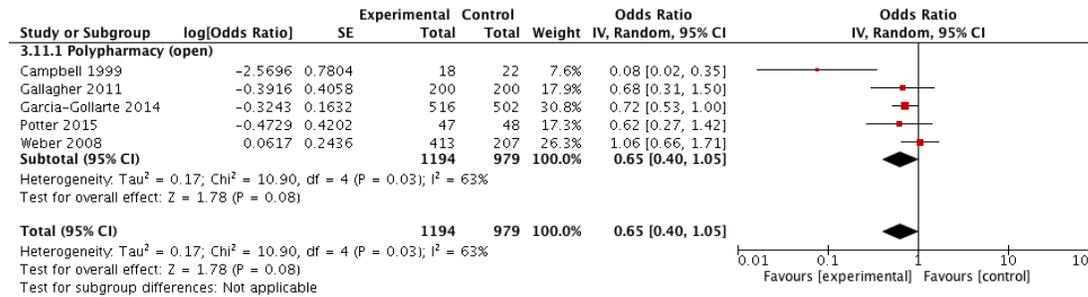
- 132 papers (n= 34143 participants) – randomised and observational studies that involved deprescribing one or more medicines in older people.
- Robust literature search and methodology
- Randomised studies that assessed impact on mortality (n=10, 3151 participants) showed no significant impact on mortality (OR 0.82, 95% CI: 0.61 to 1.11) however when restricted to interventions applied at the individual patient level (n=8, 1906 participants) it was associated with a reduction in mortality (OR 0.62, 95% CI: 0.43 to 0.88). Educational interventions has no impact (OR 1.21 (0.86 to 1.69)
- Non-randomised studies (n=2, 257 participants) showed a significant decrease in mortality (OR 0.32, 95%CI: 0.17 to 0.6)
- Subgroup analysis based on age, single medication/class withdrawal, cognitive status showed no significant differences in terms of impact on mortality/

# Other findings

## Mortality associated with deprescribing interventions to reduce antipsychotic medications in randomized studies

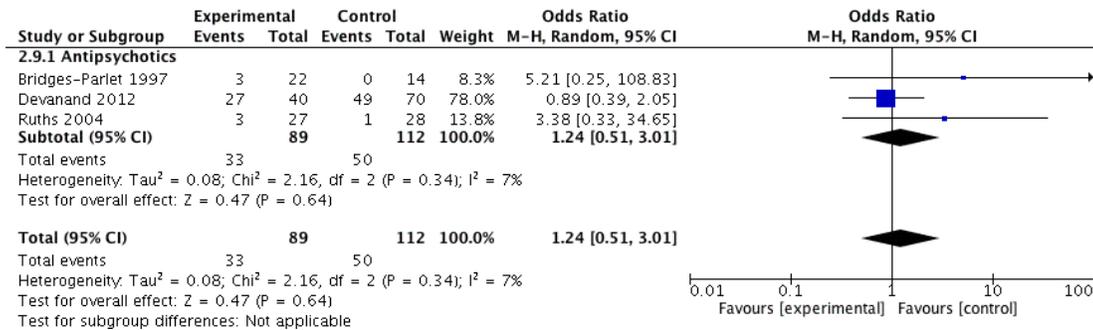


## Number of falls per participant associated with deprescribing interventions to reduce polypharmacy in randomized studies

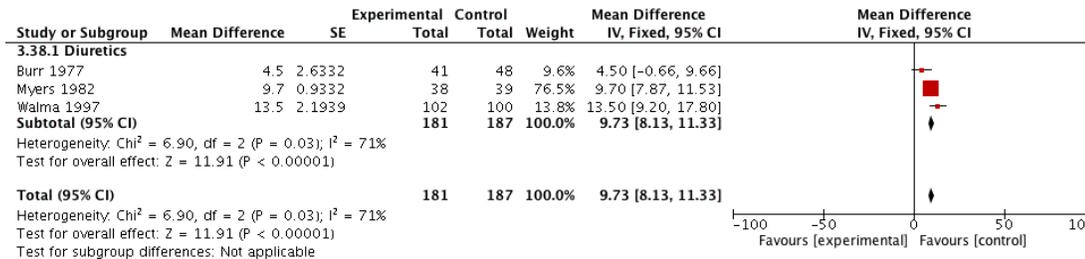


# Other findings

## Adverse drug withdrawal effects associated with deprescribing interventions to reduce antipsychotic medications in randomized studies

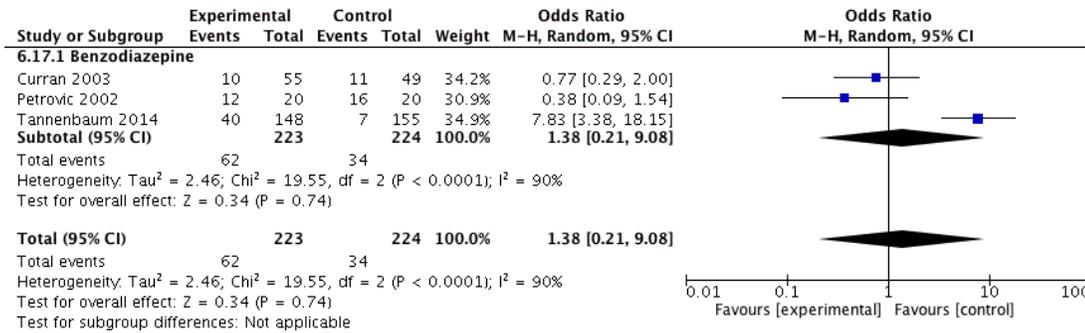


## Systolic blood pressure associated with deprescribing interventions to reduce diuretics in randomized studies

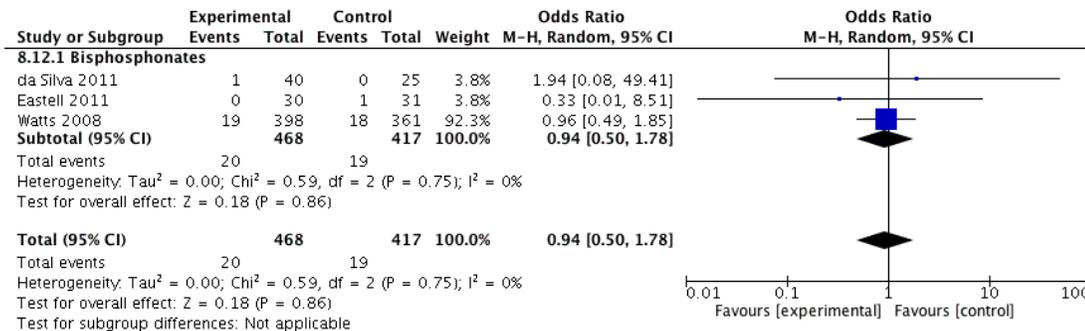


# Other findings

## Successful withdrawal associated with deprescribing interventions to reduce benzodiazepine use in randomized studies



## Non-vertebral fractures associated with deprescribing interventions to cease bisphosphonates in non-randomized studies



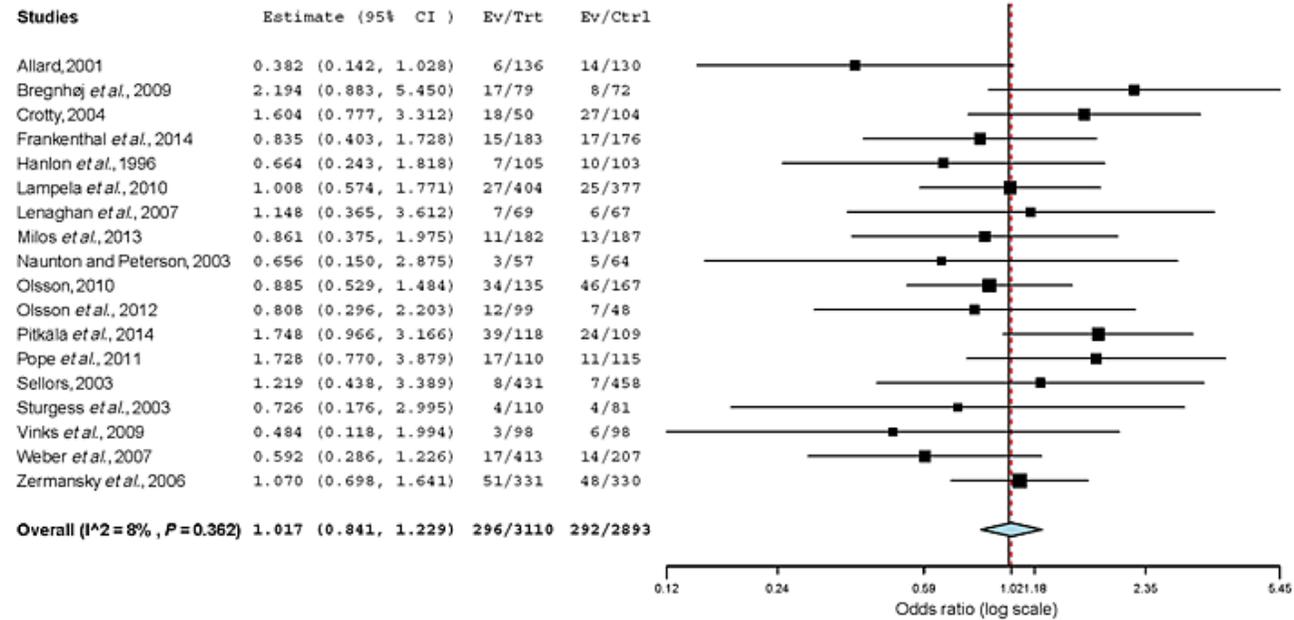
# Evidence that it isn't harmful

**Impact of strategies to reduce polypharmacy on clinically relevant endpoints: a systematic review and meta-analysis**

**Br J Clin Pharmacol. 2016; 82: 532-48**

Twenty-five studies, including 10 980 participants, were included, comprising 21 randomized controlled trials and four nonrandomized controlled trials

# Impact of strategies to reduce polypharmacy on clinically relevant endpoints: a systematic review and meta-analysis



# Evidence that it does some good

Interventions to improve the appropriate use of polypharmacy in older people: a Cochrane systematic review.

BMJ Open 2015; 5: e009235.

12 studies (n= 22438 - 8 RCTs, 2 cluster RCTs and 2 controlled before and after studies)

# Evidence that it does some good

- Impact on hospital admission
  - 2 studies reported no impact, 3 studies reported some reduction. Meta-analysis not possible
  - Similar finding reported in BJCP meta-analysis – 2 studies positive, 6 studies no significant difference and no meta-analysis possible
- Improvement in mortality?
  - BJCP meta-analysis based on low quality evidence estimated that for every 1000 patients that undergo a strategy to reduce polypharmacy – a statistically non-significant 5 less patients will die within the a follow up period of between 2 and 18 months (but 95% CI extends from a reduction of 16 deaths to an increase of 22)

# Evidence that it does some good

- Improvement in medication appropriateness
  - Based on 4 RCTs -summated MAI score (-)6.78, 95% CI (-)12.34 to (-)1.22. But marked heterogeneity – I squared- 96%
  - Based on 2 studies – intervention patients prescribed fewer Beers drugs than control patients. Mean difference (-)0.1 (95% CI: (-) 0.28 to (+) 0.09 but marked heterogeneity
  - Two studies assessed impact on STOPP medicines both showed a reduction but data not pooled
  - BJCP analysis – showed a difference in the number of inappropriate medicines prescribed of 0.49 (95%CI: 0.28 to 0.7) (3 studies – 839 participants)

# Evidence that it does some good

- Reduction in number of medicines taken
  - BJCP meta-analysis reported a mean reduction of 0.99 medicines per patient (95%CI: 0.14 to 1.83) (based on 2 studies and 451 participants)
- Impact on quality of life
  - In general - no evidence that deprescribing is associated with significant changes in quality of life using standardised measures although one study showed a significant but modest impact in terms of slowing decline in quality of life (MD 0.3 – 1 study, 189 participants)

# Stopping PPIs

- Deprescribing versus continuation of chronic pump inhibitor use in adults. Cochrane Database Systematic Reviews 2017; Issue 3
  - Review of 6 trials with 1758 participants
  - 5 trials assessed on-demand prescribing and 1 assessed sudden cessation
  - Low quality evidence indicates that on-demand use increases risk of “lack of symptom control compared with continuous use (RR 1.71 – 95%CI 1.31 to 2.22)
  - Moderate quality evidence that on-demand use leads to a reduction in pill burden of 3.79 doses per week (2.84 to 4.73)
  - Low quality evidence that on-demand dosing is associated with reduced patient satisfaction

# Stopping bisphosphonates

## **FDA - Background Document for Meeting of Advisory Committee for Reproductive Health Drugs and Drug Safety and Risk Management Advisory Committee (2011)**

- Limited fracture data on bisphosphonate exposure out to 10 years appear to demonstrate that there is sustained but no further increase in fracture benefit after 3-4 years of therapy but also no clear evidence of harm or increase in overall osteoporotic fractures. While different subsets of patients appear to have evidence of benefit with continued therapy, these findings are dependent on the study reviewed. There is no clear subset of patients that has clear benefit with continued therapy confirmed across multiple studies. In patients who discontinue bisphosphonate exposure after 3-5 years of treatment, fracture incidence rates were relatively constant over time.

# Stopping antihyperglycaemics

Lack of evidence to guide deprescribing of antihyperglycaemics: a systematic review. *Diabetes Ther*; 2017: 23-31

- Only 2 controlled before and after studies – both deemed to be low quality
  - One study of an educational intervention aimed at pharmacists showed that use of glibenclamide could be reduced (by switching or stopping) without compromised glycaemic control in community-dwelling older people [actual difference 0.06% in HbA1c – 95%CI: -0.16 to 0.12%] (n= 4368)
  - One study showed that if oral antihyperglycemics and insulin ( $\leq 20$  units per day) were discontinued (or if  $>20$  units reduced by 50%) in nursing home residents (n=32) there was a non-significant 1.1% (0.56% lower to 1.64% higher) increase in HbA1c and no significant impact on mortality (RR 0.74, 95%CI: 0.29 to 1.87).

# STOPPFrail: consensus validation

- Published in Age and Ageing 2017; 46: 60-627
- List of potentially inappropriate prescribing indicators in older patients ( $\geq 65$  years) who meet all of these criteria
  - End stage irreversible pathology
  - Poor one year survival prognosis
  - Severe functional impairment and/or severe cognitive impairment
  - Symptom control is the priority rather than prevention of disease progression

# List of medicines for review includes

- Lipid lowering medicines
- Alpha blockers for hypertension
- Anti-platelets for primary prevention
- Neuroleptics antipsychotics
- Memantine
- PPIs and H2 antagonists
- GI antispasmodics
- Theophylline
- Calcium supplements

# List of medicines for review includes

- Antiresorptive, SERMs and bone anabolic medicines
- Long-term NSAIDs
- Long-term corticosteroids
- Diabetic oral agents – aim for monotherapy
- ACEIs or ARBs for prevention diabetic nephropathy
- Multivitamins
- Nutritional supplements
- Prophylactic antibiotics

# The economics of deprescribing

Health economics analysis of polypharmacy reviews  
([www.polypharmacy.scot.nhs](http://www.polypharmacy.scot.nhs))

- Estimated that number of patients aged 75 years and older, receiving a high-risk medicine and estimated to be at 40-60% risk of admission/readmission equates to 747 patients per 100,000 population
- Additionally estimated that number of patients aged 50 years and over resident in a care home and taking medicine equates to 580 per 100,000 population
- As a combined population potentially eligible for medication review this equates to 1221 per 100,000 population (ie 1.2% population)

# The economics of deprescribing

## Cost avoidance

- If one drug with an average unit cost of £9.87 (and an average 6 repeats) is stopped for one year – this would reduce prescribing costs by ~£72,000 per 100,000 population (of which ~£45,000 is in the over 75 years cohort)
- If two drugs are stopped these estimates are doubled (ie £144,000 per 100,000 popn of which £90,000 is in the over 75's cohort)
- If cost estimates extended to include switching to more cost effective medicines and removal of duplicate prescriptions cost avoidance increases to between £109,000 and £189,000 per 100,000 population.
- It is estimated that the cost of hospitalisation due to avoidable ADRs is between £58,500 and £407,000 per 100,000 population

# The economics of deprescribing

## Costs incurred

- If we assume a review requires 1.46 hours pharmacist time, 0.63 hours physician time and 0.5 hours of nurse/pharmacist to undertake implement and follow-up – this equates to £114 per review including on-costs.
- Based on previous numbers this requires £140,000 per 100,000 population of staff time (of which £89,000 is focussed on 75+ years cohort)
- Bottom line – even focussing on the highest risk populations the costs avoided and costs incurred are likely to be similar unless reviews lead to a reduction in health service utilisation (especially hospitalisation) and/or include a wider consideration of cost-effective prescribing.