

**Appendix 1: Selected studies that have examined drug discontinuation**

Drug [publication]	Design and objectives	Subjects	Findings
Digoxin [ <i>Lancet</i> 1977; 310:1054-5]	Trial to assess cardiovascular symptoms at 2, 6, and 12 weeks after drug discontinuation	24 patients in a general practice who had been prescribed digoxin for longer than 3 months	<ul style="list-style-type: none"> <li>• Six patients with atrial fibrillation continued using digoxin</li> <li>• Digoxin was stopped in 17 of 18 patients in sinus rhythm; their cardiovascular symptoms did not worsen</li> </ul>
Diuretics [ <i>BMJ</i> 1997; 315:464-8]	Randomized trial to assess proportion of patients who can be successfully withdrawn from diuretics	202 elderly patients in general practice taking long-term diuretics without heart failure or hypertension	<ul style="list-style-type: none"> <li>• Diuretic reinitiation was required in 50 patients (49%) in the withdrawal group and 13 (13%) in the control group</li> <li>• Heart failure was the most frequent reason for reinitiation</li> <li>• Cessation of diuretics was associated with mean increase in systolic (13.5 mm Hg) and diastolic BP (4.6 mm Hg)</li> </ul>
Antipsychotics [ <i>N Engl J Med</i> 1992;327: 168-73]	Randomized trial of educational intervention to reduce use of psychoactive medicines	823 elderly residents in 6 matched pairs of nursing homes	<ul style="list-style-type: none"> <li>• Psychoactive drugs were discontinued more frequently in residents of experimental (32%) than control sites (14%)</li> <li>• Most measures of clinical status did not differ significantly between the 2 groups</li> </ul>
Anticonvulsants [ <i>Lancet</i> 1991; 337:1175-80]	Randomized trial of drug discontinuation to assess rates and risk factors for recurrence of seizures	1013 patients with epilepsy taking AEDs who had been seizure-free for $\geq 2$ years	<ul style="list-style-type: none"> <li>• At 1–2 years of follow-up, those whose AEDs were discontinued had a higher recurrent seizure rate (41%) than controls (22%)</li> <li>• Associations with relapse rate were found for a history of tonic-clonic seizures, remission length and taking <math>\geq 2</math> AEDs</li> </ul>
Multiple meds [ <i>Arch Intern Med</i> 1997; 157:2205-10]	Chart review of ADWEs	Elderly patients	
	From a controlled trial, to determine frequency, severity and the factors associated with ADWEs	124 general-medicine outpatients within a single Veterans Affairs system who were taking $\geq 5$ medications daily	<ul style="list-style-type: none"> <li>• 26% of drugs stopped led to ADWEs</li> <li>• Drugs most frequently associated with ADWEs were those affecting the cardiovascular and central nervous systems</li> <li>• 36% of ADWEs led to a hospital admission, a trip to the emergency department or an urgent-care visit</li> </ul>
	To determine types, severity, frequency, timing and the factors associated with ADWEs	175 consecutive people admitted to an academic Veterans Affairs nursing home	<ul style="list-style-type: none"> <li>• 62 patients experienced 94 ADWEs</li> <li>• Independent risks found for ADWEs included having more diagnoses, taking more medicines and hospital admission(s) while residing in the nursing home</li> </ul>

Note: BP = blood pressure, meds = medications, AEDs = antiepileptic drugs, ADWEs = adverse drug-withdrawal events.