Tapering Medication
What, When, How

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Education and Research Days

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Who?

- Clients in the last hours to days of life
- Clients with progressive terminal disease
What?

- Non essential
- Difficult to administer
- Patient refuses
- Withdrawal symptoms not likely
- Risk greater than benefit
When?

- Patient says
- Physician says (or does)
- Team says
- Patient unable (delirious, restless)
- PPS
- Bedbound
- Oral or IV routes unavailable
How?

- Consult patient and family
- Taper
- Cold Turkey
- Offer PRN’s
- Plan ahead, monitor, have back up plan
WHY?

- QOL
- Comfort
- Dignity
- Shift Resources
- “Give death a chance”
  - PCF4  www:palliativedrugs.com
Specific reasons WHY

- Interactions
- Side Effects
- Covert medication administration.
- NNT data
- Research: PIP, IP, Seniors, LTC, “Polypharmacy”
- Co-morbid disease Δ (renal, dementia, cardiac, Parkinson's, MS, depression, diabetes)
Covert Medication Administration - What is it?

• Administration without the patient’s knowledge, agreement or understanding.
  – Secrecy-pill in a sandwich
  – Ethical? Paternalistic?
  – If team, relatives and carers say so
    • Blue Sky; One Flew Over the Cuckoo’s Nest
Covert Medication – how do we do it in palliative care?

- In food
- Switched to liquid format
- Switched to topical format
- SC
- Crushed
- In tube feeds
  - does pt want it or not, is it safe or convenient?

- Steinhauer M. 2004 Wisconsin Resident Care
Covert Medication Guideline

• Aim: consider best interest of patient
  – have discussion
  – make intent and implications of treatment clear
• Aim-: guide team and carers-Issue a position statement
  – eg: “prevent deterioration, ensure improvement in physical or mental health”*

• Tapering or reducing may avoid covert admin.

• *Nurses and Midwives Nov 2007 UK
More WHY’s
Drug Interactions

- How do we apply the risk/benefit formula?
- Are we monitoring closely and can risk combinations?
- One drug of concern: methadone
Drug Interactions & Methadone (M)

- Good charts available; electronic systems may not pick up interactions
- Inducers decrease methadone
  - Removal=↑M after 2-3 wks
- Inhibitors increase methadone
  - Removal=↓M rapidly (hrs to days)
- ♥↑QTc >100mg/d approx (varies)
Methadone Inhibitors

(increase methadone levels)

• Ciprofloxacin, diazepam, metronidazole

• (Some examples of commonly used drugs in our clients)
Methadone Inducers

Reduce methadone levels

• Phenobarbital, carbamazepine, phenytoin, spironolactone, dexamethasone (16-24mg)

• (Some examples of commonly used drugs in our clients)
Methadone & QTc Interactions

- Clarithromycin, keto/flu conazole, haloperidol, methotrimeprazine, sertraline, citalopram, olanzapine, TCA’s

- (Some examples of commonly used drugs in our clients)
Tapering while patient on Methadone

- Keep methadone (pain management priority)
- Remove interacting drug - cleanest option
- Taper or reduce interacting drug if essential (eg: decadron)
Another WHY
NNT data is suspect in our clients

• NNT omits the denominator of TIME
• Not the same to treat 100 people for 5 years as it is to treat 500 people for 1 year
• Relationship is non-linear; and in declining health; eg: cachexia, ↓PPS harm risk is increased
  • Currow D Arch Int Med 2006
• Many of these studies did not include our client population; patients with progressive (often cancer) disease
Tapering in Comorbid illness

- Depression, kidney disease, dementia, cardiac, diabetes, parkinson's, MS
- We need structured evidence base to assist with prescribing in comorbid diseases.
  - Stevenson J. JPSM 2007
Comorbid Prescribing Psychiatric Drugs

• *Process of drug withdrawal* of antidepressants and antipsychotics is the cause of problems, not return of illness.
  • Moncrieff J, Medical Hypothesis 2006

• Palliative Care psychiatrists, must target symptoms as PART of diagnosis & medications used must have evidence in dying patients.
  • Irwin S. Pall and Supp Care 2009
Comorbid prescribing & end stage renal failure stage 5 or d/c dialysis

- New symptoms: pain and agitation require medications
  - Fassett R. Nephrology 2011
- Symptom control, pain discussion, which opioid, NHS – Framework for CKD
  - Russon L. Clinical medicine 2010 Vol 10
- d/c phosphate binders, calcium & vit D, warfarin, statins, erythropoietin
Comorbid Dementia Prescribing

• 34% had or were taking inappropriate medications (Delphi process)
  • Holmes H. J Am Ger Soc 2008

• 21% continued on acetylcholinesterase inhibitors and medications such as memantine
  • Weschules D, J Palliat Med 2008
Discontinuing Statins in Comorbid Arthrosclerosis

• No difference in survival with or without statins
• Missed opportunity to reduce therapeutic burden and limit health care spending

Discontinuing Statins cont’d

- 50% lung cancer patients received statin at death
- Lipid monitoring sub-optimal
- Lipid goal rarely achieved
  - Tanvelyanon T. J Palliat Care 22:2006
- Should be first to be discontinued
  - PCF4 www:palliativedrugs.com
Discontinuing Warfarin

- Patients anxious- compliance has been heavily monitored
- “Straightforward to d/c” last days of life (Risk of stroke @ EOL< other risks of therapy)
  - PCF4 www.palliativedrugs.com
Tapering Digoxin

- Renal failure requires reduction and d/c
- d/c when prescribed for sinus rhythm
- d/c in AF if patient tolerates
  - PCF4 www.palliativedrugs.com
Comorbid Hypertension

? Tight control?

i.e. not 140/90

• Incorporate “real world” clinical principles “check in”; use algorithm & exempt patients with the following:
  – Adverse effects, 4+ AHT meds, terminal disease, mod/sev dementia or other, comfort care, poor adherence.
    • Steinman M. Goldstein M. JC Accred. 2011
• D/C when pt moribund/comatose –(LCPPathway)
• “Inappropriate in end stage disease”
  • PCF4 www.palliativedrugs.com
Comorbid Thrombotic Risk (PTP= thromboprophylaxis)

- PTP guidelines for cancer patients based on level 1A evidence
- ARE NICE guidelines appropriate? Patients with progressive disease largely excluded from the studies!
- PTP Should be considered in reversible pathology
- Consider bruising, infection and site avail.

- Gillon S Palliative Medicine Aug 2011
Tapering in Parkinson’s & MS

- **Pain** will require additional medications
  - Central, neuropathic, spastic pain
  - National Guidelines promote EOL shift
- Comfort vs “control function”
- Terminal event often an acute sepsis
- Hallucinations may respond to med reduction
- Sudden levodopa withdrawal → NMS
- Midazolam CSCI may be necessary
  - Campbell C. Jones E Merrills J; Ontario Health
Tapering and comorbid diabetes

- Emotional (like warfarin)
- d/c insulin when unconscious (PCF4)
- HbA1c inappropriate (long term SE not relevant)
- Just avoid symptoms of hyper or hypo glycemia
- Treat patient not serum glucose levels
More WHY’S
1. Side Effects

- Deserve **greater** emphasis at end of life
- NNT data not applicable
- Frameworks needed to guide care @ EOL which consider side effects
  - Harper A. BMJ 2004
2. The Evil of Polypharmacy

- Recognized negative effect on patients
- Vitamins, antihypertensives, hypoglycemics and chronic illness drugs need 2\textsuperscript{nd} look
  - Goh C SMJ 2002
- Dementia patients benefit from reduction of medication load, reduction in mortality and improved QOL
  - Garfinkel D. IMAJ June(9) 2007
Polypharmacy in the Elderly Cancer Patient

- Clinical pharmacist on interdisciplinary team - tested communication
- 47 patients - polypharmacy was common
  - 13% had medication “errors”
  - 53% needed regime changed
  - 28% had inappropriate meds d/c

- Flood K. A J Ger Phar 2009
3. Research supports need to taper and reduce

- Seniors, LTC
- EOL
- Female
Seniors Overmedicalized

• Kept on prevention drugs unnecessarily
  – Antihypertensives
  – Statins
  – Sedatives for management
  – Medicalized sexual dysfunction
    – CMAJ Aug 9, 2011 (183)
Care Home (LTC) Inappropriate prescribing

• Systematic Review of effective interventions & interventional strategies guidelines for prescribing, education including academic detailing show promise.  Loganathan M

• Reduction of antipsychotics in dementia as they are not appropriate for chemical restraint & non drug measures effective.  Meeks T.
Potentially Inappropriate Prescriptions (PIP)

• 1716 residents – 48% one IP, 18% two IP
  • Ruggiero C. ULISSE Project Italy

• 2345 residents - 45% inappropriate prescribing according to Beers or McLeod criteria.
  • Stafford A. J Clin Pharm and Ther 2011

• 338,801 pts - STOPP - 36% PIP
  – Polypharmacy, Duplicate
  – Proton Pump Inhibitors (>8 wks); NSAIDS (> 3 mo);
    LA BDZ (> 1 mo)
    – Br J Clin Pharmacol 69:5 2010
EOL and tapering preventative medication

- Chronic disease medication is continued despite questionable benefit.
- Need to add preventative palliative medications- increasing list
- Consensus criteria should be developed for inappropriate medication use
  - Maddison A. Progress in Palliative Care 2011
Many patients have medications that contravene the Beers’ Criteria


Medications for co-morbid medical conditions should be reviewed in context of their original therapeutic goals.

- Older participants took more medications.

Poor Older or Female & Tapering or Reducing Benzodiazepines

• “2852 participants; use rarely in accordance to guidelines; duration too long; old and ill most vulnerable.
  – BJ Clin Pharm 71:2 2011”

• Long term use by 3.5% B.C. population
  – Female, lower income, older and poorer health status
  – BC Administrative database Cunningham C. 1996-2006
NSAID & PPI in Hospital patients

- 388 patients 15% on NSAID
  - 66% on PPI
  - 40% had stage 2/3 CKD
  - 35% had Ischemic HD
  - 35% other meds GI risk
  - 32% pts with 1 risk on PPI
  - 425 pts with 3 or 4 GI risk on PPI

Kitchen J. July 2008
Criteria for d/c or taper

- **Beers**: identifies medications to have potential risks (adverse outcomes and prescribing concerns) that outweigh potential benefits of the drug for > 65 years of age, regardless of their level of frailty.

- **STOPP** (French), **START** (Australian) and **CPC** (Norwegian) offer drug-drug interaction, omission of beneficial therapy and broader international criteria consideration.

- **LCP** - Liverpool Care Pathway
  - Useful as checklist, narrows the list of medications
  - We can then ask question: “What is the purpose of THESE medications in our patient at THIS time?”
Beer’s –HPC applicability

- 2003 list 33 drugs
- Amitriptyline, barbiturates, belladonna alkaloids, clonidine criteria not relevant
- List helpful as highlights side effects usually seen
Discontinuation of Multiple Medications Systematically

- Used an algorithm “Good Palliative-Geriatric Practice”
- 70 pts, avg age @death 89y
- Successful discontinuation in 81% (311 meds)
- 88% reported improved global health!
  - Garfinkel D. Arc Int Med 2010
STOPP & START criteria

- 400 patients, significant improvements in prescribing appropriateness were sustained for 6 months after discharge
  - Gallagher P. Connor M, Mahony D
# Taper Table Examples

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>WITHDRAWAL SYMPTOMS</th>
<th>CLASS AFFECTED</th>
<th>PLAN FOR TAPER</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. BACLOFEN</td>
<td>Mild: body aches, anxiety, sweats, insomnia, Severe: delirium, HTN, tachycardia</td>
<td>YES-MUSCLE RELAXANTS</td>
<td>taper over 1-2 weeks</td>
</tr>
<tr>
<td>2. CITALOPRAM</td>
<td>muscle aches, N/V, diarrhea, dizziness, irritability, insomnia, &quot;electric shock&quot; to body</td>
<td>YES- SSRIs</td>
<td>tapered over 3 to 4 weeks, reduce dose by 25%/week,</td>
</tr>
<tr>
<td>3. CLONIDINE</td>
<td>rebound HTN, anxiety, sweats, insomnia, tachycardia, headache, tremor</td>
<td>NO</td>
<td>tapered over 2 days</td>
</tr>
<tr>
<td>4. OXAZEPAM</td>
<td>anxiety, sweats, tremor, insomnia</td>
<td>YES- BENZODIAZEPINES</td>
<td>tapered by 25% per week. If drug taken less than 3 wks, d/c theoretically possible. Switch or Long half life benzodiazepines a possibility.</td>
</tr>
<tr>
<td>5. PREDNISONE (if duration of therapy &gt;14 days)</td>
<td>Mild: N/V, headache, hypotension, muscle/joint aches Severe: adrenal crisis</td>
<td>YES- CORTICOSTEROIDS</td>
<td>half dose Q2d until 7.5mg/d, then 2mg/week. For most corticosteroids, &lt;14d can d/c Dexamethasone d/c 2-4mg q 1-7d Tapering sequence is empirical &gt;14D HPA axis suppressed &gt;++ wks HPA axis suppressed 12 mo</td>
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<tr>
<td>6. ANTICHOLINERGICS</td>
<td>Akathisia, anxiety, rhinitis, sweating,</td>
<td>YES</td>
<td>Observe, may occur few days to few weeks after d/c. Reduce q3d, over 1-2wk, or treat sx (benztropine, benzodiazepine)</td>
</tr>
<tr>
<td>7. ANTICONVULSANTS</td>
<td>Seizures, arrhythmia, tremors</td>
<td>YES</td>
<td>Observe, plan for alternatives PRN, or reduce gradually. (Phenytoin and Valproic q 2 days; Carbamazepine q 2-4 wk)</td>
</tr>
<tr>
<td>8.ANTIHISTAMINES</td>
<td>Insomnia, agitation, malaise</td>
<td>YES</td>
<td>May occur up to 7 days d/c Suggest taper if been on high doses for long periods</td>
</tr>
<tr>
<td>9.ANTIPSYCHOTICS 1ST GEN</td>
<td>++ GI, tremors, agitation ,anxiety</td>
<td>YES-</td>
<td>Occurs 1-2d post d/c. Offer alternatives PRN or reduce gradually</td>
</tr>
<tr>
<td>(eg: chlorpromazine)</td>
<td>(as per anticholinergics also)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10..ANTIPSYCHOTICS 2ND GEN</td>
<td>As above and abnormal movements</td>
<td>YES-</td>
<td>As above; eg reduce weekly</td>
</tr>
<tr>
<td>(eg: clozapine)</td>
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<td>11. BETA BLOCKERS</td>
<td>Related to indication: tachycardia</td>
<td>YES</td>
<td>Occur within 1-3 wks d/c; taper if possible</td>
</tr>
<tr>
<td>12. COCAINE</td>
<td>Sleep, hunger, dysphoria,</td>
<td></td>
<td>MAY OCCUR RAPIDLY. Symptom management</td>
</tr>
<tr>
<td>13. GABAPENTIN</td>
<td>Headache, tremors, GI; and similar to benzodiazepines</td>
<td></td>
<td>May occur 24 hours post d/c. Reduce dose if possible or offer PRN alternatives for symptoms such as benzodiazepine</td>
</tr>
<tr>
<td>14. OPIOIDS</td>
<td>Initial anxiety, sweating, ; later nausea, GI, pain</td>
<td>YES</td>
<td>w/d gradually. (10% q7d); Occurs 6 h; morphine, resolves 7D. Occurs 2 days methadone resolves 7 wk (is clonidine a subscript?) Psychological w/d may last months. Monitor, taper offer alternatives</td>
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<td>15. NICOTINE</td>
<td>Depression, insomnia, anxiety</td>
<td></td>
<td>Nicotine Patch/gum alternatives Buproprion (Zyban) – takes 2 wks onset Varenicline (Champix) - titrate up</td>
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<td>16. ANTIPARKINSONONIAN MEDICATIONS (LEVODOPA, AMANTADINE, OTHER DOPAMINERGIC AGENTS)</td>
<td>Exacerbation of extrapyramidal symptoms, confusion, hallucinations,</td>
<td></td>
<td>Taper gradually</td>
</tr>
<tr>
<td>17. SNRI (Venlafaxine)</td>
<td>Asthenia, dizziness, headache, insomnia GI, agitation, feeling of electric shock</td>
<td>Yes</td>
<td>Can occur very rapidly (with missed dose) .Withdraw over 2-6 wks</td>
</tr>
</tbody>
</table>

- Care Beyond Cure  Chapter 31 Available from [www.cshp.ca](http://www.cshp.ca)
- Davison P. Drug withdrawal .Hospital Pharmacist Dec 2007
- Baumrucker S. The Ethics of Withdrawing Treatment: How Should the Choice be Made?  AJ HP Medicine June 2006
Example cont’d

BACLOFEN

• Mild: body aches, anxiety, sweats, insomnia.

• Severe: delirium, hypertension, tachycardia

• taper over 1-2 weeks
<table>
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<th>Initial anxiety, sweating</th>
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<td>later nausea, GI, pain</td>
<td>w/d gradually.(10% q7d); Occurs 6 h morphine, resolves 7D. Occurs 2 days methadone resolves 7 wk (is clonidine a substitution?) Psychological w/d may last months. Monitor, taper offer alternatives</td>
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Withdrawal

• Most drugs when withdrawn can result in symptoms of anxiety or restlessness.
Summary

• Cold Turkey - some evidence
• Taper - some evidence
• Medication lists too long - some evidence
• Inappropriate prescribing - some evidence
• Communication is key
• What is purpose of this drug now?
• What is your understanding of your disease now.