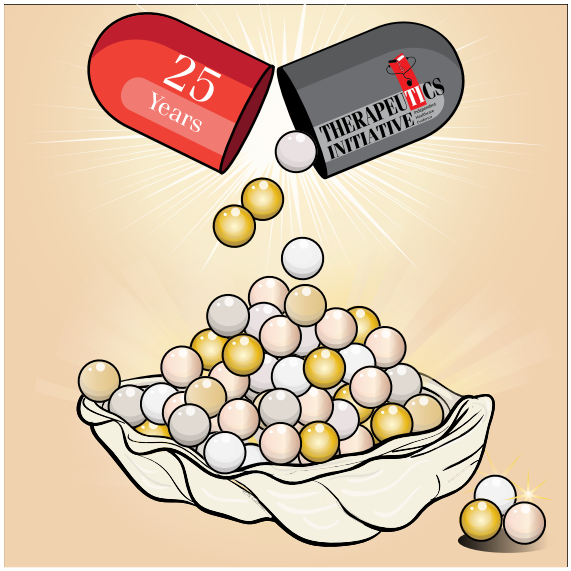
THERAPEUTICS INITIATIVE Evidence Based Drug Therapy

Twenty-Five Pearls from 25 years (part 2)



In this Letter, the second in a 2-part anniversary series, we present the remaining 12 "clinical pearls" found in Therapeutics Letters published between 2006 and 2018. The Therapeutics Initiative is celebrating its 25th anniversary this year, in part by highlighting some key conclusions from the 120 issues of the Therapeutics Letter published so far.

14 The majority of new drugs do NOT represent a major advantage when compared to available alternatives

Increasing drug costs: Are we getting good value? [Apr-Jul 2006, issue **59**]. This Letter estimated that "if the increased use of 'me-too' drugs in Canada could be stopped for just one year, we could save more than one billion dollars …" Thus, prescribers, administrators, and government bodies collectively have the power to prevent this waste and free up money for other sectors of the healthcare system.

15 Risk assessment tools need to be studied in RCTs

Using Framingham for primary prevention cardiovascular risk assessment [Mar-Apr 2007, issue **63**]. This Letter reported on a systematic review of 17 epidemiologic studies assessing the accuracy of the Framingham risk scores, which concluded that scores were inaccurate, tending to underestimate risk in high risk populations and overestimate risk in low risk populations.

16 Health care professionals must know how to critique and verify drug information in news stories

Evaluating the media as a source of drug therapy information [Nov-Dec 2007, issue **67**]. This Letter provides examples of how media stories can be misleading and concluded that **"Frequently therapeutic effects are neither as spectacular nor as disastrous as media headlines suggest."**

17 Better benefit and harm evidence is needed before long-term CNS stimulants can be recommended for treatment of ADHD in children

What is the evidence for using CNS stimulants to treat ADHD in children? [Mar-May 2008, issue **69**]. Short-term CNS stimulants improve teacher and parent ratings of hyperactive/impulsive disruptive behavior but do not improve children's ratings of anxiety or measures of academic achievement. Later, ***Stimulants for ADHD in children - Revisited*** [Jan-Feb 2018, issue **110**] concluded that **"there is convincing evidence that a proportion of boys and girls treated with stimulants in BC and around the world are simply the youngest in their class, and at a different developmental stage than earlier-born classmates."** This "birth month effect" has been confirmed in BC research and around the world.

18 Statins do NOT have a proven net health benefit in primary prevention and their role in this setting should be reconsidered

Do statins have a role in primary prevention? An Update [Mar-Apr 2010, issue **77**]. The reduction in major CHD serious adverse events with statins compared to placebo is not reflected in a reduction in total numbers of people with at least one serious adverse event.

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19 There are no clinically meaningful benefits of bisphosphonates in postmenopausal women with NO prior fracture or vertebral compression

A systematic review of the efficacy of bisphosphonates [Sep-Oct 2011, issue 83]. Because of the small magnitude of effect and the high risk of bias in the included trials, this Letter concluded that in women with a prior fracture or vertebral compression, **"it is unclear whether bisphosphonates cause a clinically meaningful reduction of hip fractures."**

20 Seven steps to become adept at deprescribing

Reducing Polypharmacy. A logical approach [Jun-Jul 2014, issue 90]. Treatments for symptoms or prevention should be re-evaluated regularly and should meet a test of common sense: **"in this patient, do the medicine's benefits meaningfully outweigh its harms?"**

21 Most commonly used surrogate markers have not been proven to be consistently predictive of morbidity and mortality

The limitations and potential hazards of using surrogate markers [Oct-Dec 2014, issue 92]. This Letter provided examples of where relying on surrogate markers to assess effectiveness of drug therapy proved to be harmful. The Letter recommends **avoiding "chasing surrogate targets (e.g. LDL cholesterol) that have not been proven to have a net health benefit."**

22 Lower blood pressure targets have not been shown to have a net health benefit

Does SPRINT change our approach to blood pressure targets? [Jan-Feb 2016, issue 98] and ***Using best evidence for the management of hypertension*** [May-Jun 2017, issue 106]. An updated analysis of 11 RCTs (including SPRINT) with over 38,000 participants showed that lower targets did not reduce total mortality, or total serious adverse events. **Blood pressure treatment targets should be the same as those used in RCTs, i.e.below 140-160/90-100 mmHg, for prevention of cardiovascular events and death.**

23 Independent analysis of Study 329 demonstrated serious harms and a lack of efficacy for acute and longer-term use of paroxetine and imipramine for adolescents with major depression

Study 329 Why is it so important? [Jul-Aug 2016, issue 101]. This Letter concluded that **"Published conclusions about efficacy and safety of drugs without independent analysis cannot be accepted as trustworthy."**

24 Growing evidence that the 'glucocentric' drug management approach for type 2 diabetes is misguided

Is the current 'glucocentric' approach to management of type 2 diabetes misguided? [Nov-Dec 2016, issue 103]. This Letter concluded that "Large long-term randomized controlled trials measuring outcomes important to patients are needed urgently to test different approaches and drugs for the management of type 2 diabetes." Also about treatment of type 2 diabetes, ***EMPA-REG OUTCOME Trial: What does it mean?*** [Jul-Aug 2017, issue 107] concluded: **"It is uncertain whether the reduction in mortality and serious adverse events in the EMPA-REG OUTCOME trial is attributable to empagliflozin or to less use of other glucose-lowering therapies."**

25 Compared to placebo the Shingrix vaccine reduced the incidence of herpes zoster

Shingrix: A New Vaccine for Shingles [Sep-Oct 2018, issue 114]. The vaccine reduced the incidence of shingles **over 3.5 years by 3.26% (NNV = 31) in all age groups and reduced the incidence of post-herpetic neuralgia by 0.28% (NNV ≈ 350).** Compared to placebo, Shingrix increased grade 3 systemic reactions (which prevented normal daily activities for about 1-3 days) by 4 to 9% (NNH 11 to 25). When considering this vaccine, the physician and patient must consider the balance of baseline herpes zoster risk, harms, benefits and costs.

The draft of this Therapeutics Letter was submitted for review to 130 experts and primary care physicians in order to correct any inaccuracies and to ensure that the information is concise and relevant to clinicians.

The Therapeutics Initiative is funded by the BC Ministry of Health through a grant to the University of BC. The Therapeutics Initiative provides evidence-based advice about drug therapy, and is not responsible for formulating or adjudicating provincial drug policies.