CTO
Thursday, November 5th
2:15pm – 3:00pm
8 minutes!

When Less is More: A Participant's Perspective on Treatment Optimisation

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My objectives

Beth is the most important person in this session!

But…

- Why, in 2026, do patients still face so much variability in care?
- Why in 2026 are researchers still trapped in a “well meaning” Health Canada-mandated system (DIN and CTAs) that makes performing research to identify optimal care next to impossible?
- **Who in this room is prepared to make a stand?**

Why is variability in oncology so common?

1

Drugs are approved at maximum doses after

Clinicians then cut doses, and drugs still work, with no regulatory approval.

2

Research funds the "new & exciting", not

Little money to compare established treatments, so we face many “reasonable” choices and never learn which is best.

3

Regulation blocks optimisation

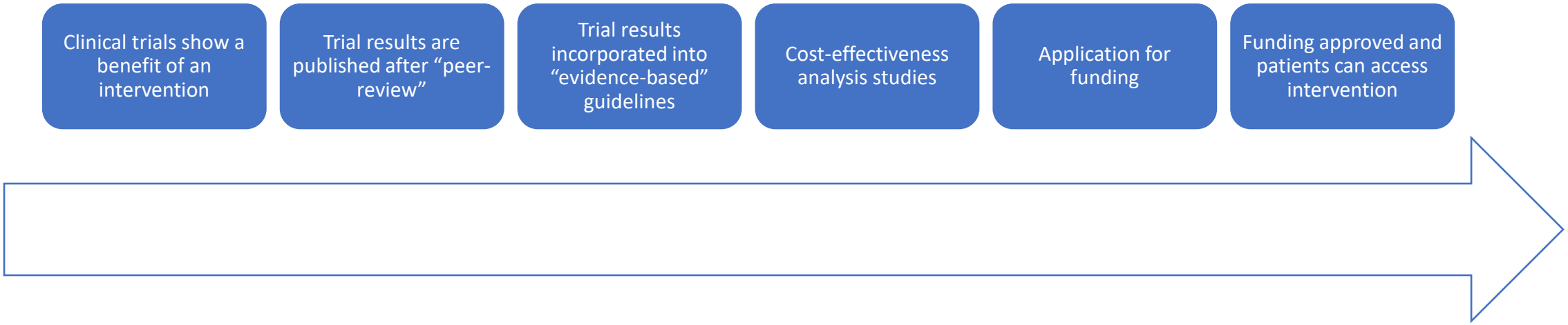
“Well-meaning” rules make dose-optimisation trials next to impossible because pharma is not going to pay for trials.

Patients and society pay the price

Is Our Current System Serving Patients Optimally?

The Traditional Paradigm Limits Practical Innovation

Highly selected patients
Doses designed to get to market fast



We almost never re-evaluate treatments based on new data

…unless the data help a pharmaceutical company

Example: bisphosphonates in breast cancer

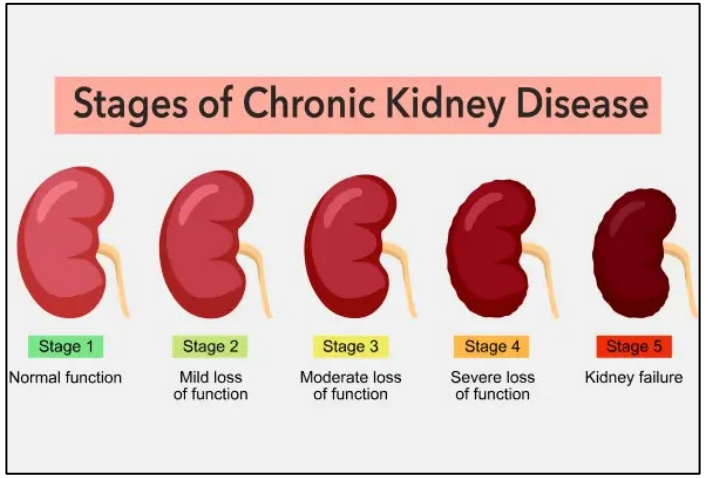
Metastatic disease

- Given every 4 weeks – despite a bone half-life of ~10 years
- 20 years to show 12-weekly works as well: less toxicity, less cost

Early breast cancer

- Trials used 7 to 19 infusions, 4-weekly to 6-monthly – none was “better than any other”
- 6-monthly for 3 years has become our standard
- In osteoporosis and AI bone loss, one zoledronate dose lasts 5 years

Are we repeating same errors as in metastatic disease?





Rare but serious toxicities

The Rethinking Clinical Trials (REaCT-ZOL trial)

- The worlds largest pragmatic cancer trials program (OHRI.ca/react)
- Randomised, multicentre, pragmatic: one dose vs. twice-yearly zoledronate for 3 years in early breast cancer

Surveys

Practice varied widely. Patients and clinicians wanted dose-optimisation trials.

The trial

Patients enrolled. 1 infusion vs 6-monthly infusions over 3 years.

The result

No difference between arms for survival outcomes.
Less toxicity with one infusion.

Final results

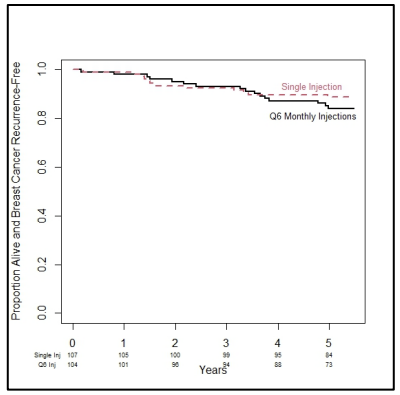
NEJM Evidence

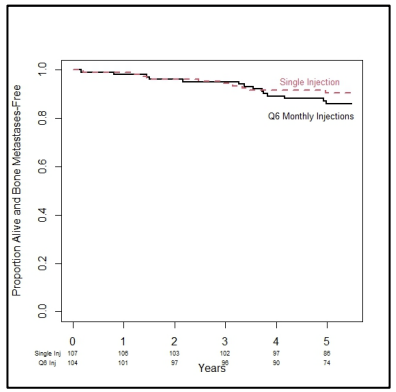
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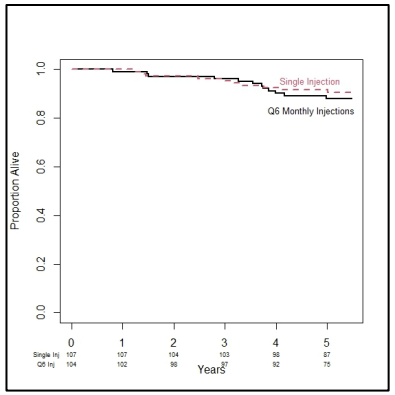
ORIGINAL ARTICLE

Every Six-Month versus Single-Dose Adjuvant Zoledronate in Early Breast Cancer

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REaCT-zol

Finding: one dose = seven doses over 3 years. No difference between arms.

Scope: 30,000 Canadian women a year (2 million globally)

The roadblocks:

1. ASCO-OH review is “swamped” by pharma – “unlikely to open the file before 2027.” A pharma-funded trial would jump the queue.

2. Product monograph won’t be updated – this stays “off-label”

3. Very few patients will be offered this treatment

It’s not drug de-escalation – it’s optimisation!

The dose we approve

Highest “tolerable toxicity” (not efficacy) in unusually healthy patients – set to get the drug to market

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The dose patients & society need

The lowest dose that works – and we’re finding it is often lower

Why we can’t simply test lower doses

No obligation

on manufacturers to update the drug’s Drug Identification Number (DIN)

A new dose = a new application

Health Canada requires a Clinical Trial Application (CTA)

Too expensive

for academic, non-pharma trials

What do we need to do as a nation?

1. **End the complacency** (everyone in this room)
   Agree that this cannot continue
   This is not just a cancer story i.e. paediatrics, rare diseases

2. **Update product monographs, DINs and CTA processes**
   Accept evidence from national guideline committees
   Despite a completed RCT, REaCT-ZOL has not been added to DIN

3. **Every time I give a lower, "optimal" dose, I am prescribing off-label**
   So very few patients will be offered this treatment

Think about that as you listen to Beth's incredible story…