Overview

- Pharmaceutical care: the philosophical underpinning of modern pharmacy practice
- The pharmaceutical care process
- Establishing a desired outcome
- Alternative solutions to patients’ drug-related problems
- The alternative therapies compromise
- Documenting patient choice, need, and effectiveness
- An overview of N-of-1 trials

Pharmaceutical Care

“The responsible provision of drug therapy by a pharmacist for the purpose of achieving specific outcomes that improve a patient’s quality of life.”

Hepler & Strand, *AJHP* 1990; 47:533-41

Establishing a desired outcome

- Outcome must be stated explicitly
- Clinical intent
  - Cure
  - Alleviate symptoms
  - Arrest or slow a disease process
  - Prevent a disease or symptoms
- Indicators of success
  - Patient indicator (symptom, lab finding, quality indicator)
  - Progress indicator (degree of improvement)
  - Desired time by which desired outcome should be seen

Alternative solutions to patients’ drug-related problems

- Do nothing
- Psychotherapy, counseling
- Nutritional approaches
- Exercise, physical therapy
- Medical devices
- Marketed drug products, legend or OTC
- “Alternative Therapies”
  - Extemporaneously compounded dosage forms
  - Alternative medicine
Risk-benefit assessment

- Goal: increase benefit
- Goal: minimize risk

- What is the risk/benefit ratio if there is no benefit?
- Who is in a position to characterize risks and benefits?
- Who is in a position to decide how much risk to experience?

The alternative therapies compromise

- Standards for production or assay may not be available
- Variability in the marketplace may be common
- Risk-benefit profile for product may not be fully understood

Basis for Alternative Therapy

- Marketed products have not been effective or are contraindicated for the patient;
- Marketed products are not tolerated by the patient;
- Marketed products are not available for the patient;
- A reasonable basis exists for supposing that alternative therapies will provide a benefit for the patient with minimal side effects;
- The decision is made within a pharmacist-patient-physician relationship;
- The patient knowingly accepts the alternative therapy compromise

Informed Consent

- Competent patient
  - Legally competent
  - Mentally competent
  - Not impaired
- Knowledge and understanding of “material facts”
  - a reasonably prudent person in the position of the patient or his representative would attach significance to [them in] deciding whether or not to submit to the proposed treatment. [RCW 7.70.050(2)]
- No duress

Material Facts in Washington

- Nature and character of proposed treatment;
- Anticipated results of proposed treatment;
- Recognized possible alternative forms of treatment
- OR
- Recognized serious possible risks, complications, and anticipated benefits involved in the treatment administered and in the recognized possible alternative forms of treatment, including nontreatment. [RCW 7.70.050(1)]

Possible elements of disclosure to patient*

- This product has been ordered by your physician
  - At your request (?)
  - At my recommendation (?)
  - Based on his experience and judgment (?)
- It is designed to have the following outcome:
- Other, marketed products, have not been effective or are not considered appropriate by your physician for you. These include:
- We prepare this product to order for individual patients. To date, we have dispensed it to ____ patients other than you.

*Presented for classroom discussion only; not legal advice.
Elements of disclosure (2)

- Unlike marketed products, this product has not been subjected to clinical testing to determine its safety in general use; there may be risks and side effects of this product that are not yet discovered.
- We exercise care in preparing this product, but we have not conducted testing to assure its stability beyond a very short time, nor do we subject this product to all of the quality control checks used for marketed products.
- We don’t know if this product will work for you, but your physician believes it may work better than other alternatives.

Elements of disclosure (3)

- The following side effects are known for the active ingredient in this product:
- Notify us or your physician immediately if you experience any of the following:
- There may be other, possibly serious side effects, that are not known and could only be discovered with controlled testing which has not been completed for this product.
- Notify your physician if the desired outcome does not occur, or if your condition worsens.

Pharmacist should document ...

- Need for alternative
- Patient’s informed consent to treatment with the alternative
- Monitoring activities to demonstrate effectiveness
- Evidence of continued need for alternative

N-of-1 Clinical Trials

- Planned trials of therapy in a single subject
- Goal is to determine most suitable treatment for a single patient
- Determine if drug works for a patient
- Determine optimum dose for a patient
- Evaluated clinically and statistically
- Require pharmacist involvement

Requirements for N-of-1 Trial*

- Condition being treated is chronic and stable
- Drug should have rapid onset of action and rapid cessation of action (ie, short half-life)
- Clinically relevant targets that can be measured
- Adequate pharmacy support
- Strategy for analysis and interpretation of results


Conduct of N-of-1 Trials

- Clinician and patient agree to test an experimental therapy for its ability to improve or control the symptoms or signs of the disease
- Treatment medication and placebo doses are prepared by pharmacist
- Randomization schedule generated by pharmacist
- Both physician and patient are blinded as to identity of medication or placebo
- Patient undergoes pairs of treatments according to the schedule
- Patient and physician record observations using a pre-agreed set of measures
- At end of trial, code is broken and treatments compared.
Reversal Designs (ABAB)

![Graph of Weekly Symptom Scores]

Alternating Treatment Designs

![Graph of Weekly Symptom Scores]

Example Patient Questionnaire*

- How much trouble or distress as a result of lightheadedness or loss of consciousness have you had during the last day?
  1. A very great deal of trouble or distress.
  2. A great deal of trouble or distress.
  3. A good deal of trouble or distress.
  4. A moderate amount of trouble or distress.
  5. Some trouble or distress.
  6. Very little trouble or distress.
  7. No trouble or distress.


Visual Inspection of Graphed Data

- Baseline and treatment scores should not overlap
- Multiple points of comparison improve confidence (e.g., at least 3 scores per phase)
- Slope of baseline diverges from slope of treatment (less stringent)

Statistical Analysis

- Paired t-tests, 2-tailed
- Mean difference of 0.5 per question (using 7-point Likert scale) indicates minimal clinical improvement*
- May also use runs test with ABAB designs

Paired T-test Analysis

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<th>Pair 2</th>
<th>Pair 3</th>
<th>Pair 4</th>
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<tr>
<td>Treatment B</td>
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<tr>
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Results of an SPT Service*

- 34 completed trials in 2 years
- 17 considered to give definitive results
- 17 showed trends only
- 16 trials favored active treatment being started or continued
- 18 trials led to discontinuance or non-initiation of therapy
- 16.5 hours of staff time per trial

*Larson, Ellsworth and Oas. *JAMA* 1993; 270: 2708

References