CLINICAL EFFECTIVENESS

Canadian
Consortium for
Early Intervention in Psychosis

Faculty

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Audience Question

What do you think Clinical Effectiveness means?

Clinical Effectiveness: ***Need for Definition***

- Limited relevance of clinical trial criteria for everyday practice

- Variations in the definition of clinical effectiveness
  - Real-life context vs. clinical efficacy trials
  - Emphasis on global functioning and other aspects of recovery vs. symptoms
  - Balance between treatment efficacy and side-effects

- Clinical effectiveness should be attempted to be applied at the individual level

Goals of Our Model

We sought to create a model that would be:

- Empirically based
- Clinically useful
- Recovery-focused
- Reflecting both the clinicians' and the patients' perspectives
- Incorporating the major societal/individual contextual elements outside of treatment that may influence person's outcome

Clinical Effectiveness

Clinical response[†] + Physical health[*]

Desired Outcome

Remission of symptoms, psychological and physical well-being[‡] sustained for a minimum of 6 months.[^]

[†] Positive, negative and disorganized symptoms
[*] Including, but not limited to medication side-effects
[‡] As measured by scales (WHO scale for physical health, sense of well-being scale)
[^] 2005 Andreasen, et al.

Andreasen NC, et al. Am J Psychiatry. 2005;162(3):441–449.

Audience Questions

Is this definition appropriate?

What would you change/add?

Is Recovery an Achievable Goal of Intervention?

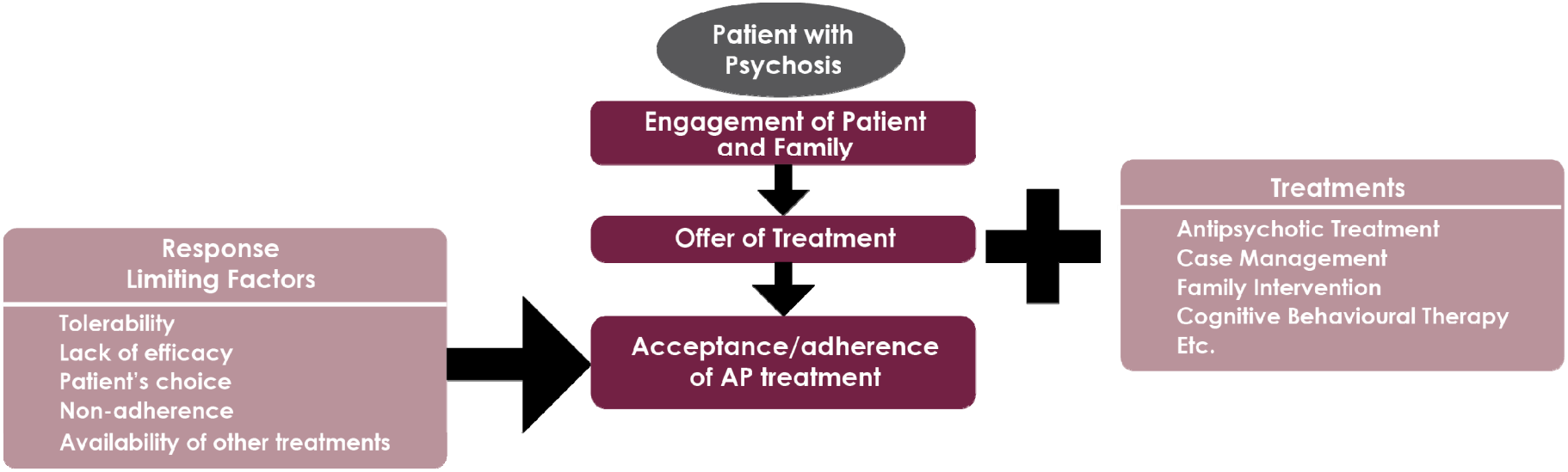
- Recovery (patient/clinician-societal definition):
  - Independent functioning and societal perspective (work, school, social relationships, independent living)
  - Relatively free of symptoms (illness perspective)
  - Personal sense of well being (physical, spiritual and existential)

Elements of the definition of recovery also constitute patient's quality of life (e.g. personal sense of well being, independent functioning)

Steps in Individualized Treatment

- Engaging patient
- Presenting the role of treatment in the context of patient's objectives
- Starting treatment
- Achieving adherence to treatment
- Improving clinical effectiveness:
  - Symptomatic response
  - Remission of symptoms with limited side-effects
- Achieving the following goals:
  - Psychological well-being
  - Physical well-being
- Sustaining these results (in particular remission)
- Reaching functional recovery

Pathway for Recovery
Patient Engagement and Acceptance



Engagement of Young People With a First Episode of Psychotic Disorder Involves:

- Initiation of contact by patient (and often family)
- Identifying problems from patient's perspective; without insisting on/or imposing a diagnosis
- Exploring patient's experiences and their own attribution of their problems
- Tolerance for substance use and not to perceive this as an obstacle (equating it with substance use in this age group in the general population)

Engagement of Young People With a First Episode of Psychotic Disorder Involves:

- Regular contact, including outreach when necessary
- Engagement of the family
- Emphasis on strengths, hope, resilience and exploration of goals and recovery orientation

Treatment

- Most first-episode patients will respond to treatment, especially if medication and psychosocial interventions are offered as a package
- Offer available antipsychotic medication based on:
  - Evidence for their efficacy
  - Safety and side-effects
  - Convenience of use (long acting vs oral, once a day vs multiple doses)
- Use of Clozapine warranted if insufficient response to two adequate antipsychotic trials (preferably within the first year)
- Presentation of a comprehensive psycho-social treatment and support:
  - Case management
  - Family intervention
  - CBT (when indicated: approximately 1/3 cases)

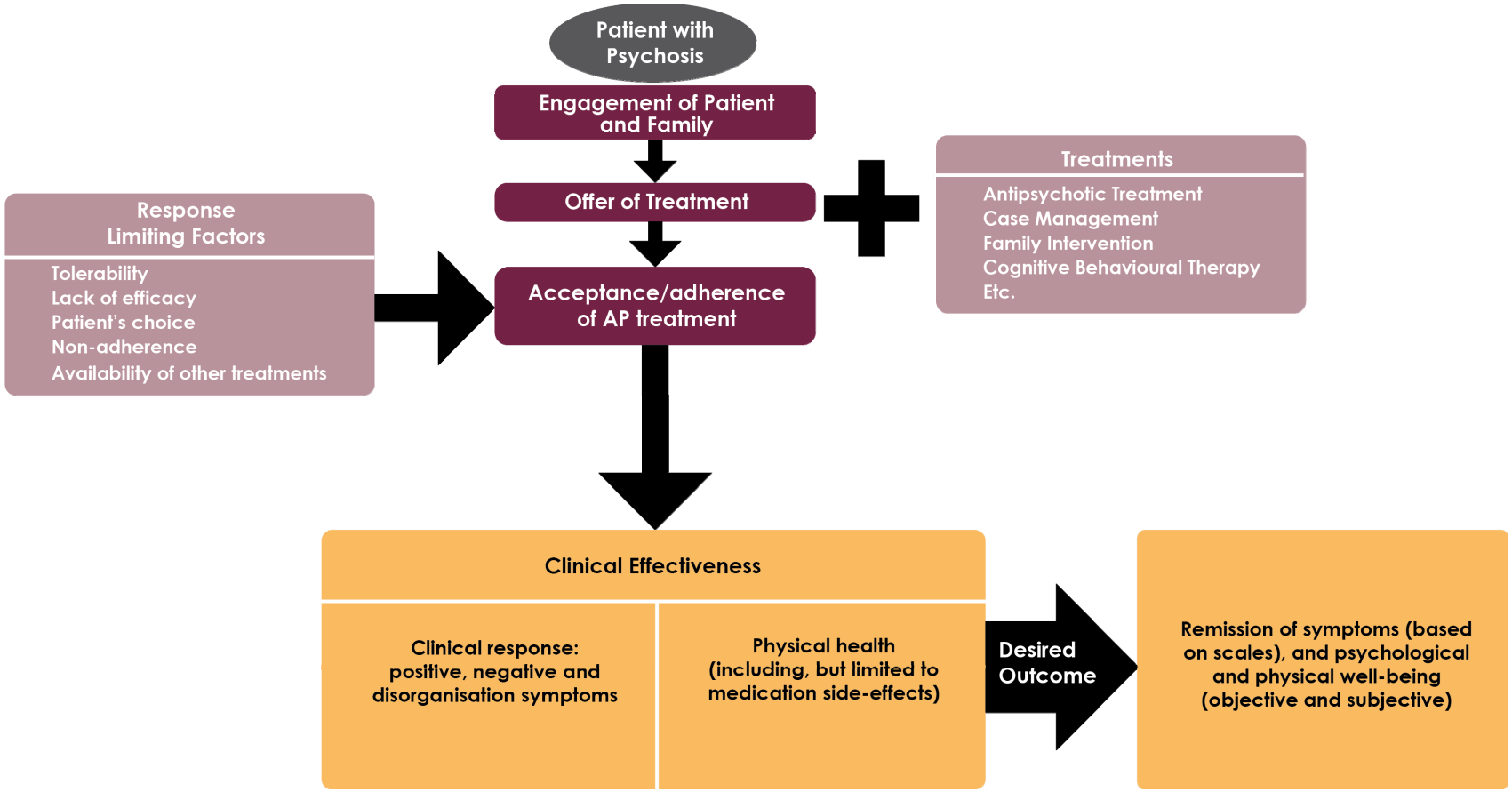
Acceptance and Adherence

- Collaborative discussions regarding treatment:
  - Exploration of patients' attitude and bias about treatment
  - Concern about short term and long term safety (e.g., "do no harm")
  - Presentation of treatment options aligned to individual goals
  - Motivational Interviewing may help to foster acceptance/adherence
- Monitoring and reinforcing adherence
- Consider and offer long-acting injectables early
- Assess and modify (if needed) treatment plan on an ongoing basis

Factors Affecting Adherence and Response

- Non-adherence:
  - Expected at every phase of illness
  - May be particularly frequent in early psychosis
- Common reasons for non-adherence include:
  - Unwillingness (willful refusal)
  - Poor engagement
  - Intolerability (weight gain, sedation, EPS)
  - Lack of efficacy
  - Patients who respond very quickly, very well (paradoxically likely to become non-adherent); hence importance of maintaining follow-up with or without medication

Pathway for Recovery: Response and Effectiveness



Response to Treatment: *Definition and Measurement*

Response: Typically assessed through the percentage decrease in severity of symptoms, hence:

- Encompasses impact on various symptoms, not only positive ones
- In clinical trials, usually a 20% reduction in total scores of scales use is considered response
- In FEP patients, 50% reduction is usually referred to as a good response

A responder according to this definition may nevertheless present fairly significant residual symptoms

Andreasen NC, et al. Am J Psychiatry. 2005;162(3):441–449.

Measurement of Response to Treatment

- May be assessed by clinician's impression and/or rating scales; the most commonly used are:
  - Clinical Global Improvement (CGI) Scale
  - Scale for the Assessment of Positive Symptoms (SAPS) and Scale for Assessment of Negative Symptoms (SANS)
  - Positive and Negative Syndrome Scale (PANSS)
  - Brief Psychiatric Rating Scale (BPRS)

Remission of Positive and Negative Symptoms

- APA consensus definition requires remission of both positive and negative symptoms
- Sustained for a period of six months
- In FEP a three month remission may be as predictive of functioning as a six month remission (Cassidy et al 2010)
- Longer period of remission is highly predictive of good functional outcome

Cassidy CM, et al. Schizophr Bull. 2010;36(5):1001-1008.

Response to Treatment: *Defining Remission*

Remission of Positive Symptoms

- Defined as a rating (on severity) of mild or no symptoms (delusions, hallucinations, thought disorder, bizarre behaviour) for a period of ranging from at least four weeks to six months (period varies across definitions)
- SAPS global rating 2 or less or for PANSS (positive symptom) items ratings of 3 or less (APA Consensus)

Remission associated with better work and social functioning

Andreasen NC, et al. Am J Psychiatry. 2005;162(3):441–449;
Jordan et al. J Clin Psychiatry 2014;75(6):e566–e572.
Malla A, et al. Psychological Medicine. 2006;null(5):649–658.

Response to Treatment: *Defining Remission*

Remission of Negative Symptoms

- Defined as a rating (on severity) of mild or no symptoms (Affective flattening, Poverty of thought, Lack of volition and motivation, Social and personal anhedonia) for a period that ranges across definitions.
- SANS global rating 2 or less or for PANSS (Negative symptom) items ratings of 3 or less (APA Consensus)

Remission of both positive and negative symptoms is associated with better work and social functioning

Andreasen NC, et al. Am J Psychiatry. 2005;162(3):441–449;
Jordan et al. J Clin Psychiatry 2014;75(6):e566–e572.
Malla A, et al. Psychological Medicine. 2006;null(5):649–658.

Tolerability of Medication Considerations

- In assessing tolerability within a clinical effectiveness perspective, one should:
  - Assess the extent to which side effects impact:
    - Subjective well-being: e.g., sedation, emotional dulling, decreased libido
    - Objective functioning: e.g., drowsiness, motor retardation, extra-pyramidal side effects
    - Physical health: e.g., weight gain, waist circumference increase, hyper-lipidemia, diabetes
  - Take into account the person's perspective
    - Some side effects may be especially disturbing for given individuals: e.g., sedation

Cassidy CM, et al. Schizophr Bull. 2010;36(5):1001-1008.

Example of a Common Scale: CGI-CB Scale

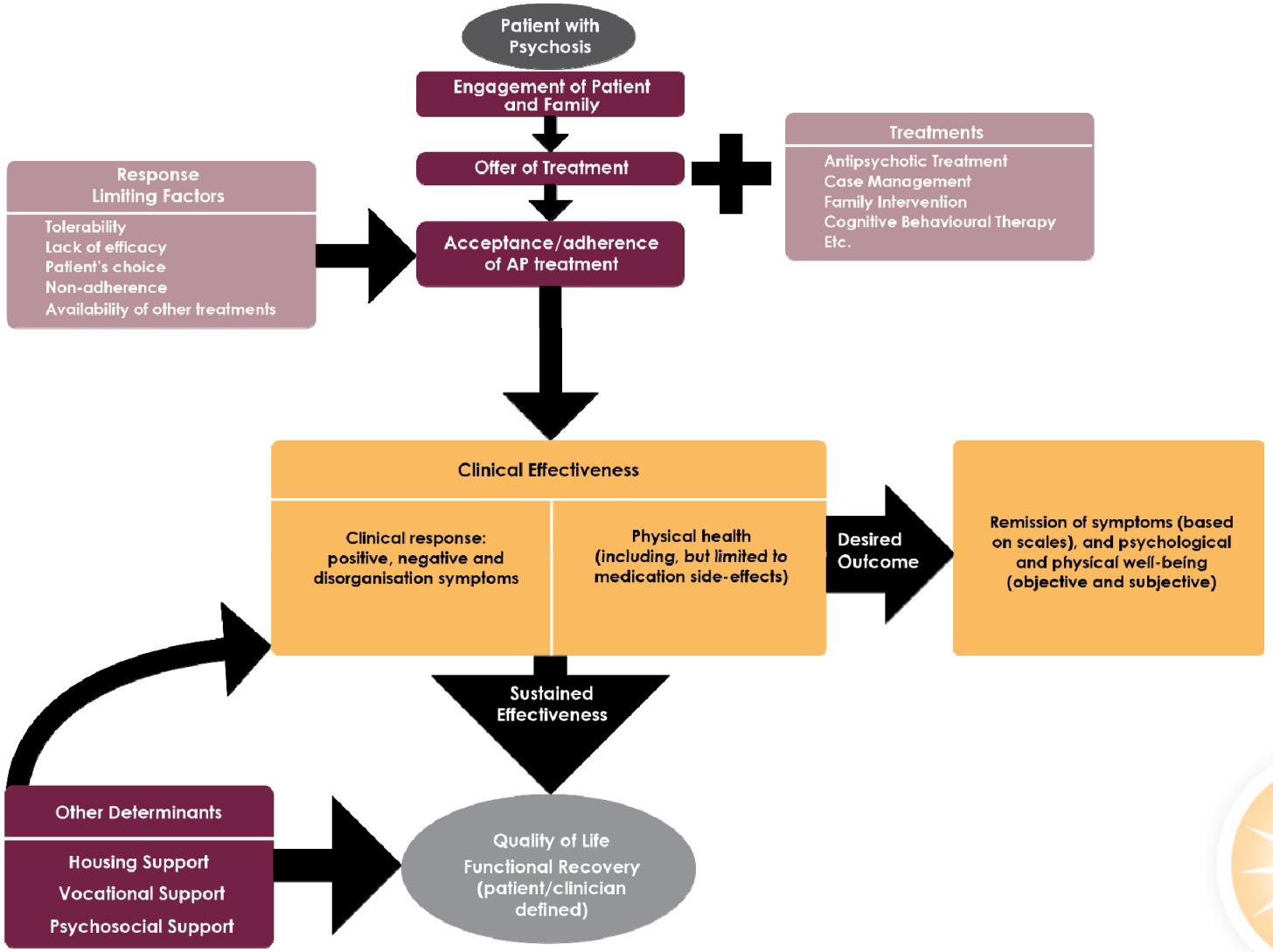
Assessment of clinical benefit using the CGI-CB scale (CGI-Efficacy Index)

	Burden of adverse events			
Therapeutic effect	**None**	**No significant interference**	**Significant interference**	**Outweighs therapeutic effect**
Marked	1	2	5	10
Moderate	3	4	6	10
Minimal	7	8	9	10
Unchanged/worse (no effect)	10	10	10	10

Rank 1 = most benefit from treatment

Rank 10 = no benefit from treatment

Pathway for Recovery



From Clinical Effectiveness to Recovery

- A high level of clinical effectiveness, i.e. achieving sustained remission with few side-effects supports progression to recovery
- Relationship between clinical effectiveness and recovery is mediated by other factors, such as pre-morbid functioning, cognition, social anxiety, self esteem, self-stigmatization, etc.
- Housing, vocational and/or psychosocial support facilitate recovery
- Recovery is also influenced by a host of other factors (family support, employment opportunities)

Windell D, et al. Psychiatr Serv. 2012;63(6):548-553.
Windell DL, et al. Soc Psychiatry Psychiatr Epidemiol. 2014;50(7):1069-1077.

Role of Factors Other Than Remission in Promoting Functional Recovery

- Cognition, hippocampal grey matter volumes and pre-morbid adjustment are capacity variables affecting both remission and functional outcome
- Better verbal memory and intact hippocampal grey matter volume may be predictive of early remission and, therefore, better longer term outcome (Bodnar et al 2008)
- There is some evidence that cognition and hippocampal grey matter volumes may be facilitated by some of the newer second generation antipsychotics such as, aripiprazole (Bodnar et al 2015)
- Corrective experiences within the context of a therapeutic relationship may provide some correction of poor pre-morbid adjustment

Bodnar M, et al. The British Journal of Psychiatry. 2008;193(4):297-304.
Hovington CL, et al. Psychiatry Res. 2015;233(3):402-408.

Audience Questions

Is the framework for clinical effectiveness of any utility to you in clinical practice?

How do you envision this framework incorporated into your practice?