

The background of the slide is a dense, repeating pattern of various colored pills and capsules. The colors include light blue, pink, yellow, and grey. The pills are scattered across the entire slide, creating a textured, medical-themed background.

The Therapeutic Alliance and Adherence in the Pharmacotherapy of Depression

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Outline

- Depression
- Adherence
- Factors affecting antidepressant adherence
 - Distress/Motivation
 - Medication characteristics
 - Treatment accessibility
 - Therapeutic alliance
 - Definition
 - “Med Backup” role
 - Elements of pharmacotherapy visit
- Improving adherence
 - Possible interventions
 - Understanding the changing role of prescribing psychiatrists and the value of “integrated treatment”

Major Teaching Points

- Antidepressant nonadherence is a frequent problem that undermines treatment effectiveness.
- Nonadherence can be addressed through attention to the medication regimen, treatment availability, and the therapeutic alliance.
- Simple interventions such as use of motivational interviewing techniques, individualizing a medication regimen to match the patients needs and values, listening actively, eliciting discussion of adverse responses, harnessing the placebo effect, providing psychoeducation, and collaborating with other caregivers can improve the alliance and secondarily improve adherence.
- Constricting a psychiatrist into the role of “med backup” denies the importance of the nonprescribing services provided by a prescribing clinician and the importance these services have in supporting the alliance and secondarily promoting treatment adherence.

Self-Assessment Question #1

Which of the following is true?

- A. Thirty per cent or more of patients discontinue antidepressants during the first month of treatment.
- B. Adherence refers to the stickiness of a pill placed in the patient's mouth.
- C. "Compliance" is preferred to "adherence" because it describes a patient's willingness to do as he or she is told.
- D. Ongoing assessment of treatment response is unnecessary in building a successful alliance with a patient.
- E. All of the above

Self-Assessment Question #2

Which of the following is true of brief (5 to 10 minute) medication visits?

- A. Clinician's ability to obtain a thorough premorbid history, history of present illness, chief complaint, and ongoing assessment of response or difficulties with medication is likely to be compromised.
- B. Therapeutic alliance is likely to be enhanced.
- C. A brief visit provides sufficient time to address behavioral symptoms, inquire about adherence and assess treatment response.
- D. Short visits foster use of medication at lower doses with briefer courses of treatment.
- E. All the above are true.

Self-Assessment Question #3

Adherence to a medication regimen is unlikely to be improved by which of the following:

- A. Listening actively and eliciting discussion of side effects
- B. Using motivational interviewing techniques
- C. Meeting for only a few minutes in order to avoid nurturing a powerful transference
- D. Refraining from communication with other clinicians whom the patient sees because splitting off the pharmacotherapy will improve treatment adherence.

Self-Assessment Question #4

Which of the following is true of the prescribing psychiatrist or nurse whose scope of activity is restricted to prescribing?

- A. A constricted role will improve job satisfaction.
- B. Delegation of psychotherapy to a nonprescribing clinician works well even when the two clinicians are critical of each others' roles and work.'
- C. Splitting of treatment roles between a prescribing clinician and a psychotherapist may not always be cost-reducing.
- D. All of the above are true.

Major Depression: A Public Health Burden

- 12-month prevalence in US 5.3 - 8.9%¹
- Lifetime prevalence in US 17.1%²
- Lifetime relapse rate 50–80%³
- Chronic course 10-20%³

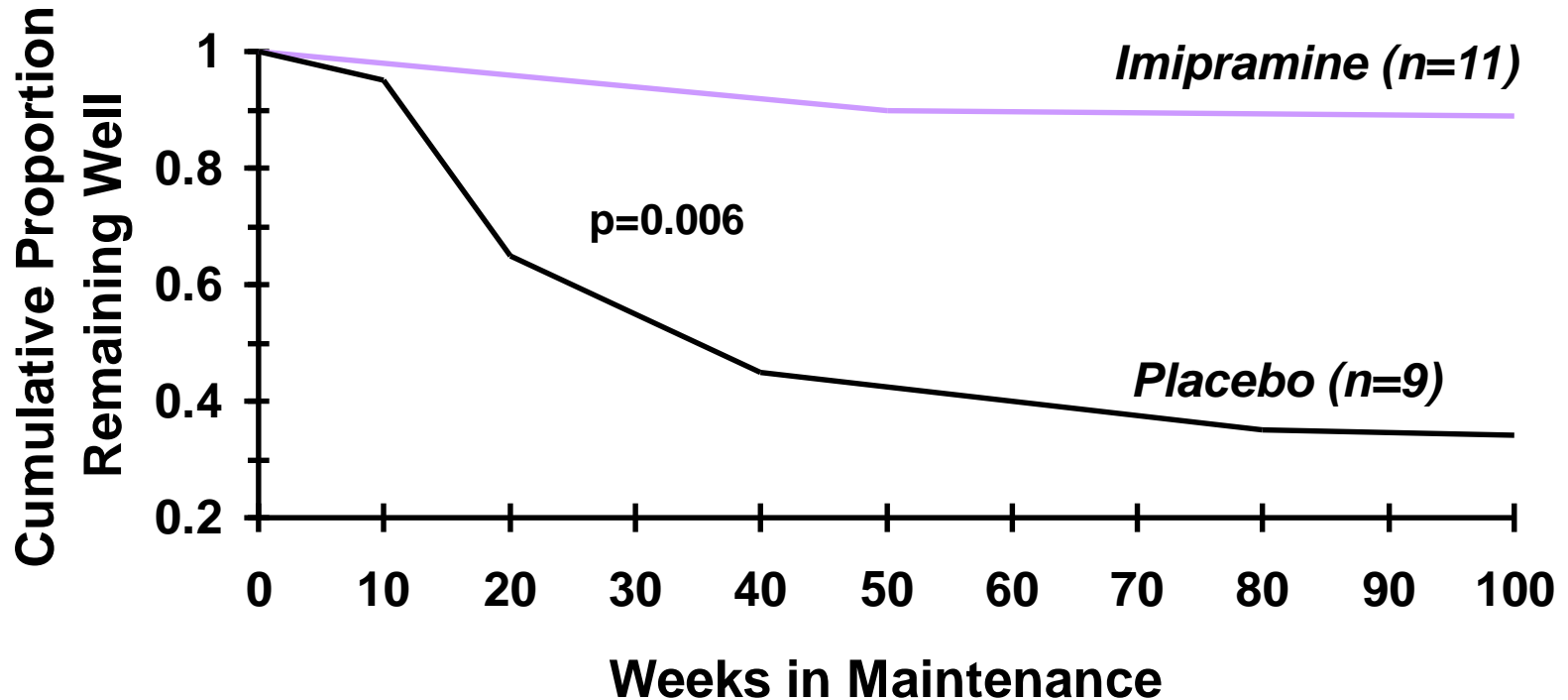
1. Satcher D, 1999: Mental Health: A Report of the Surgeon General;

2. Blazer et al. 1994; 3. Katon et al 2001

Why Is Depression Disabling?

- Suffering
- Functional impairment
- Lengthy duration of episodes
- High rate of recurrence
- Increased mortality
- Cost to family, caregivers, society

Antidepressant Maintenance Effectively Lowers the Risk of Recurrence of Depressive Episodes*

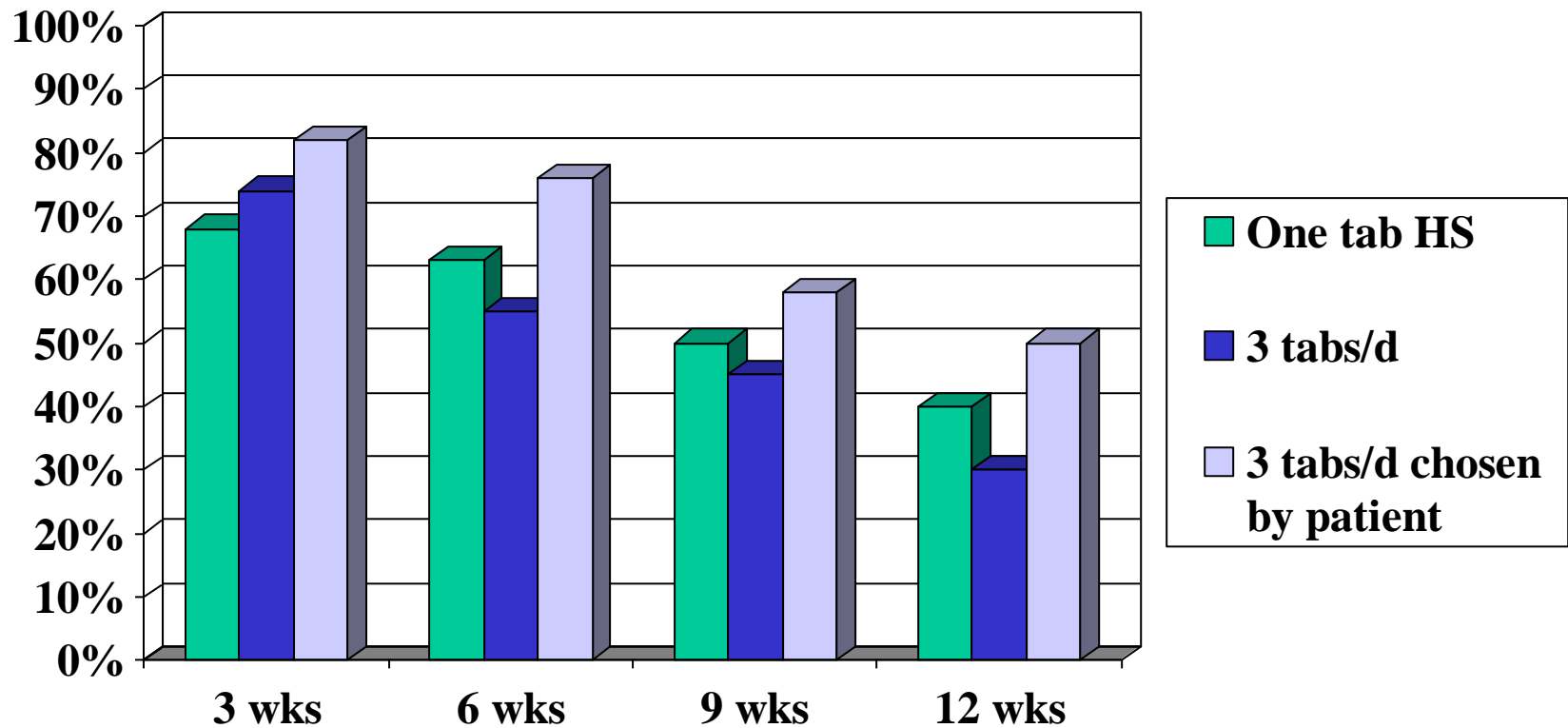


*Patients with no recurrence during a 3-year, full-dose maintenance trial were randomized to 2 years of imipramine or placebo.

Adherence: Definition and Importance

- Adherence: the degree to which a patient participates in a treatment plan
- Different emphasis from “compliance”, which emphasizes following of an order.
- Limited adherence to pharmacotherapy regimens:
 - Of 750,000,000 prescriptions written in the US and UK each year, 520,000,000 go unfilled¹
 - In depression, 30% - 68% of patients discontinue their antidepressant after 1 month²

Outpatient Adherence To Antidepressant Regimen Decreases with Complexity and with Time*



*though adherence may be greater when patient elects regimen
Myers and Branthwaite, Br J Psychiatry 1992;160:83-6.

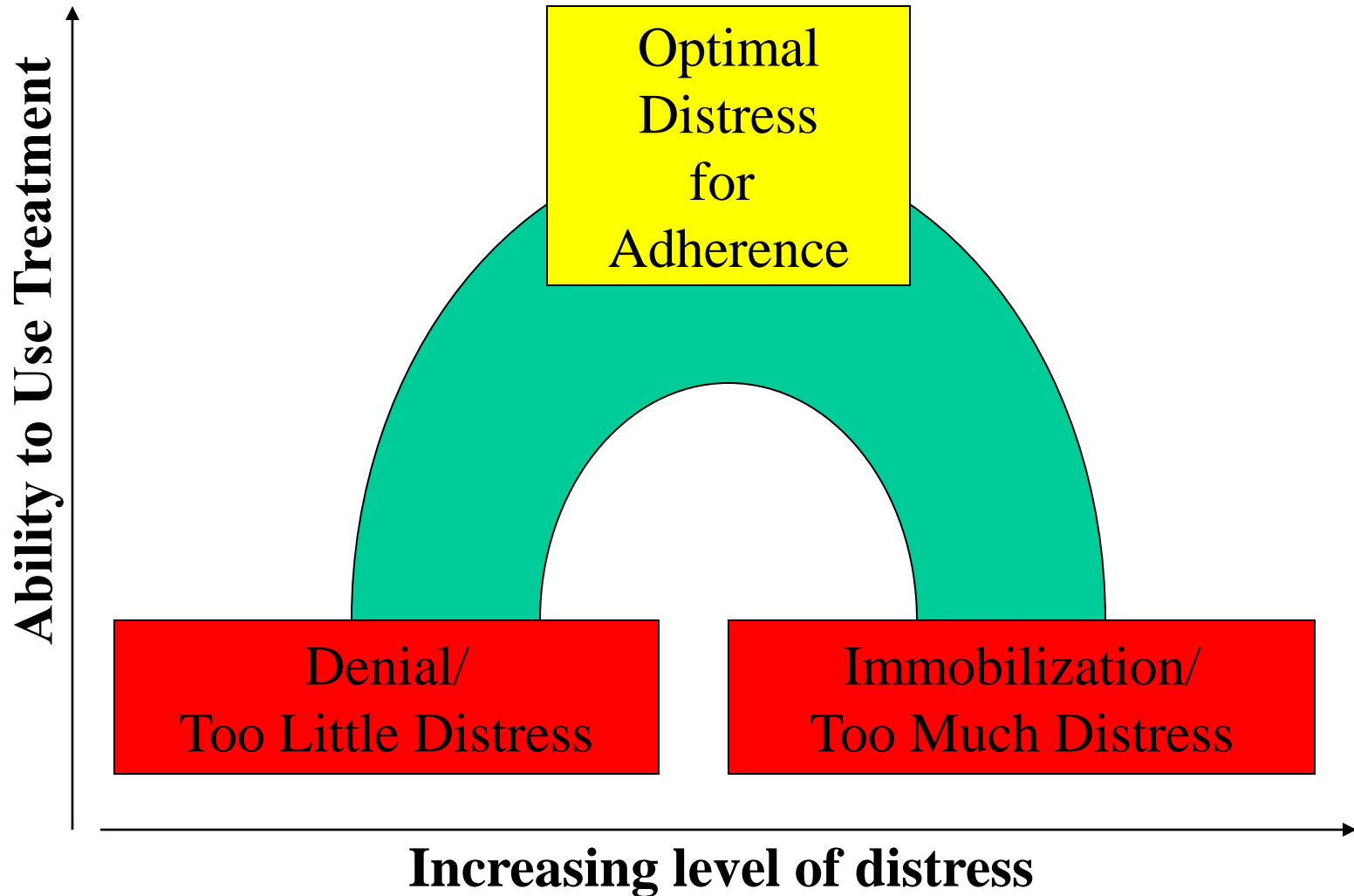
HEDIS Data Shows Poor Achievement of Minimum Recommended Antidepressant Treatment Duration

- Data from 230 health plans (122,552 lives):
- 41.2% of depressed patients failed to receive 3 months of acute treatment
- 57.8% of depressed patients failed to receive 6 months of treatment

Influences on Adherence to with Antidepressant Regimen

- Distress/Motivation
- Medication characteristics
- Treatment accessibility
- Therapeutic Alliance

Level of Distress and Motivation



Medication Characteristics



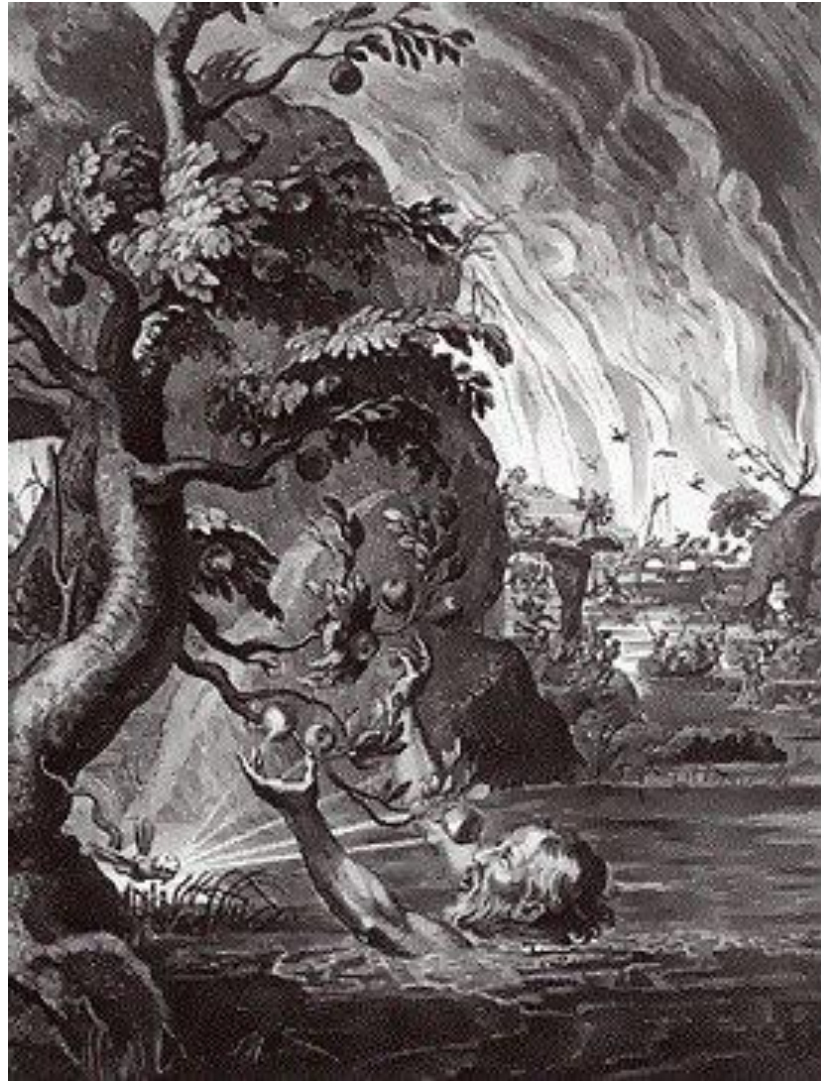
Effectiveness and Side Effects: Limitations of Current Agents

- 10%-20% of patients fail to tolerate an initial antidepressant trial¹
- Response rate in controlled trials: 55-70%²
- Typical symptom improvement: 50-75%²
- Typical remission rates: 33-50%
- Many responders live with
 - Partial improvement
 - Adverse effects

Side Effects: What **Else** Does the Antidepressant Alter?

- Sleep and Alertness
- Appetite and weight
- Motivation and energy
- Concentration, Memory, Speech fluency
- Sexual libido and performance

Treatment Accessibility



Barriers to Access

- Healthcare delivery system
 - Actual availability of treatment (e.g. phantom networks)
 - Restricted choices (e.g. push toward medications)
 - Benefit limitations (e.g. formulary choices)
 - Treatment costs (e.g. copayments or fees for service)
- Poor support group
 - Spouse, employer
- Patient's lifestyle
 - Cited as factor by patients more than by psychiatrists¹

1. Warner et al 1994

Increasing Reliance on Antidepressants in US Treatment of Depression (1987 to 1997)

- Proportion of population receiving outpatient treatment for depression has increased (0.73 to 2.33%)¹
- Antidepressant use has increased (37.4 to 74.5%)¹
- Psychotherapy (71.1 vs 60.2%) and mean number of psychotherapy visits decreased (12.6/yr to 8.7/yr)¹
- Increasing copayments for psychotherapy cited as factor in increased reliance on antidepressants.²

Therapeutic Alliance



Therapeutic Alliance

- “Collaborative bond between therapist and patient”¹
- Significantly influences treatment outcome in pharmacotherapy of depression¹
 - Holding environment
 - Enhancer of placebo effects
- Specific “pharmacotherapeutic alliance”
 - Safe and supportive interaction
 - Communication
 - Education
 - “Participant prescribing” vs simple dispensing of meds²

1. Krupnick et al. 1996;2. Gutheil 1978.

Rise of the “Med Backup”

- Precedents
 - Therapist/Prescriber split in psychoanalysis
 - Community Mental Health Team model
- Need for Specialization due to increased treatment options
- Resource management in managed care systems:
 - Response to patient demands
 - Efficient allocation of costly staff resources
 - Psychotherapy can be provided by range of clinicians

What Does a Psychopharmacologist Do?



Elements of a Pharmacotherapy Visit

1. Review previous records
2. Establish rapport/consent
3. Obtain interval history
4. Assess treatment response
5. Assess mental status
6. Update treatment plan
7. Educate re diagnosis and treatment
8. Address questions/concerns
9. Write prescription
10. Arrange tests/consultations
11. Schedule next visit
12. Document visit/new plans
13. Complete additional paperwork/letters
14. Liaison with other care providers/family

Why Are Brief Appointments Conducive to Poor Treatment?

- Hurried clinician will:
 - Lack knowledge of patient history
 - Lack perspective on degree of variance from baseline
 - Be hampered in forming treatment alliance
 - Lack sufficient time for observing current behavior, inquiring about adherence, or assessing treatment response
 - Tendency to increase medication number/dosages and prolong treatment if risk-averse
 - Lose professional satisfaction

What Can We Do To Increase Adherence?



1. Address Level of Distress and Motivation

- Assess patient for suitability of diagnosis/symptoms for treatment.
- Assess level of denial/motivation.
- Use motivational interviewing techniques to ally with patient around target symptoms.

2. Address Medication and Treatment Regimen Characteristics

- Match regimen to patient's needs:
 - Cost
 - Simplicity/Scheduling
 - Side effect profile
- Monitor effects and side effects in ongoing way
- Offer alternatives when appropriate

3. Address Accessibility of Treatment

- Assess availability of prescriber.
- Assess affordability of care.
- How does life routine help or hinder?
- How does social support system help or hinder?

4. Strengthen the Therapeutic Alliance

“...the proper use of drugs actually depends on the existence of a psychotherapeutic relationship.”¹

A. Reduce “Hurry” through Allocation of Visit Time

Activity in “Med Check” Visit	30-Min Session	15-Min Session
Open ended questions	15	5
Follow-up questions	5	2
Specific questions regarding treatment response	3	2
Specific questions and discussion of adverse effects	2	2
Discussion of treatment plan	2	2
Patient education	2	1
Prescription	1	1

B. Listen Actively to Identify Patient Requests/Needs

“A patient may come to us saying, ‘I’m here for an antidepressant’... We may say, ‘Tell me about your sleep, your appetite, your interest in sex’... We may fail to say, ‘Tell me about your depression’... We need to appreciate the patient’s experience and what it means to this person”.

Silk K, in Tasman, Riba, Silk (eds). The Doctor-Patient Relationship in Pharmacotherapy: Improving Treatment Effectiveness. Guilford Press, 2000.

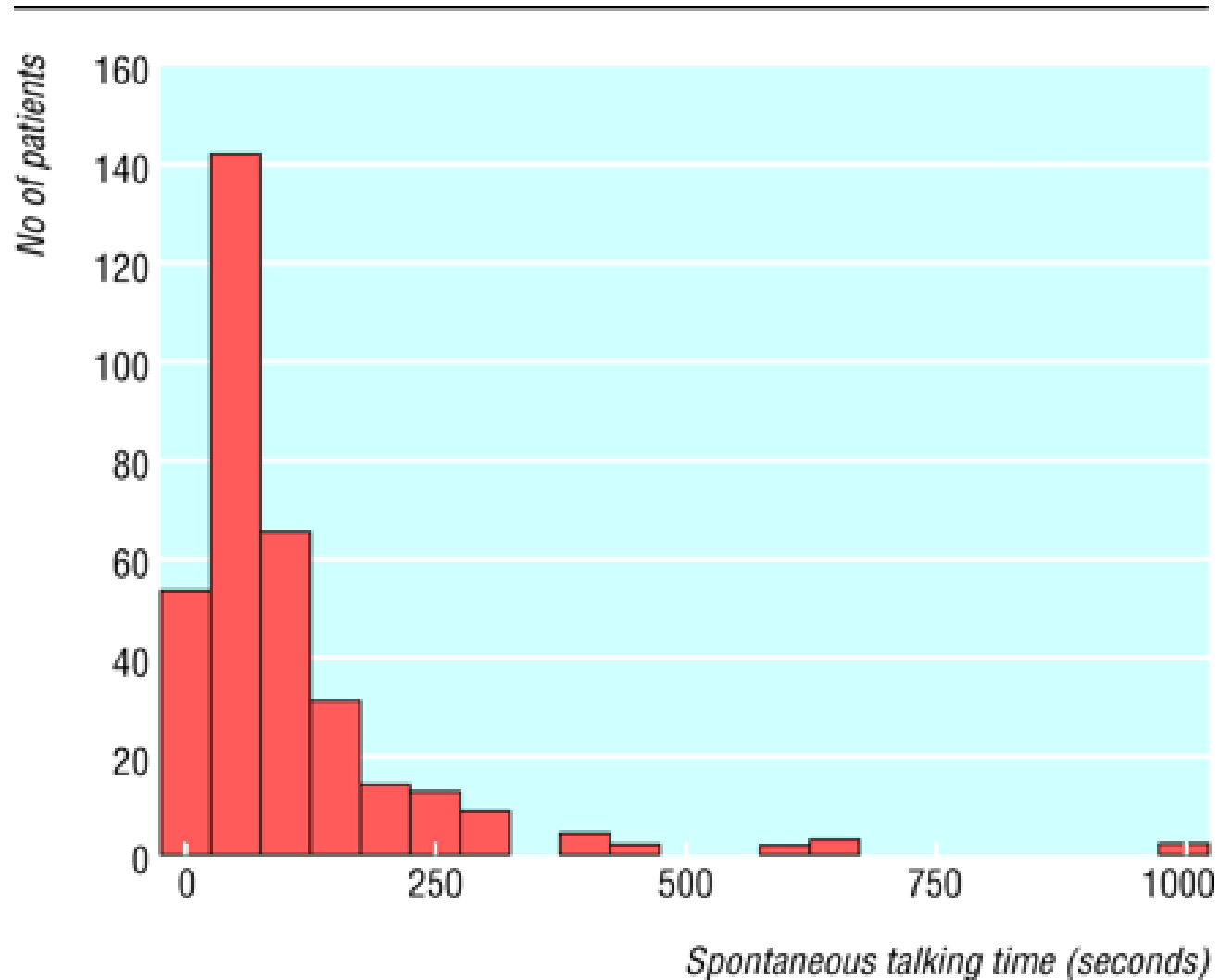
Identify Patient's Request

- Following 82 new psychiatric initial appointments in outpatient clinic, only 65% returned for second appointment.
- A predictor of return was patient's sense of "feeling understood in the initial session".¹
- Restating patient's request conveys shared therapeutic goals, strengthens alliance.

Allowing the Patient's Spontaneous Report¹

- Average US patient is interrupted after 22 seconds¹
- Spontaneous report duration in 335 medical outpatients:²
 - Mean uninterrupted spontaneous talking time was 92 sec.
 - 78% of patients finished in less than 2 min.
 - Age, but not other demographics, affected this.

Spontaneous Talking Time of Uninterrupted Outpatients



Langewitz et al. BMJ 2002;325:682-3

Listen to Adverse Events

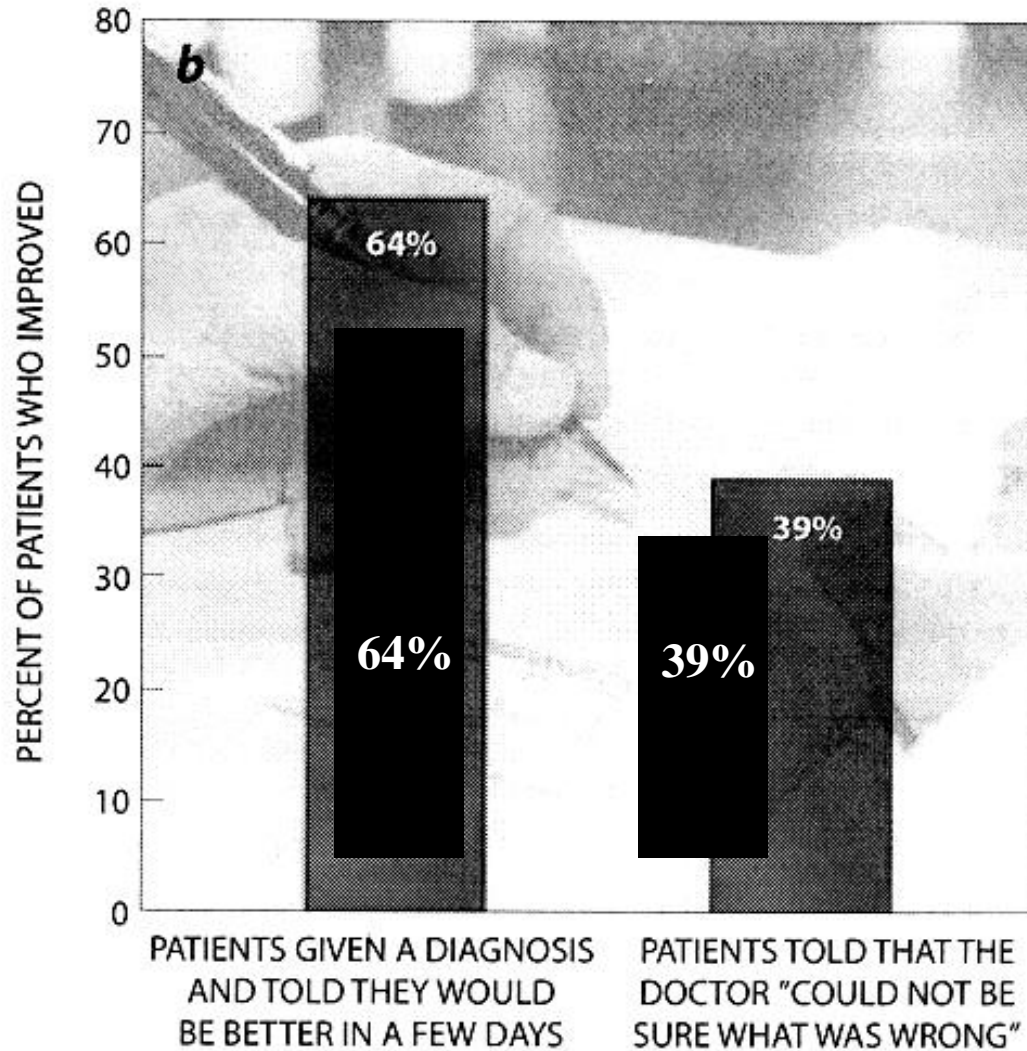
- In a telephone survey of 401 Kaiser patients treated for depression, those who reported discussing adverse events with their physicians were:
 - Half as likely to discontinue therapy (0.49)
 - More than five times as likely to switch medications (OR 5.6)

C. Harness the Placebo Effect

- Placebo effect in depression ranges from 30 to 70%¹.
- Identify a problem
- Demonstrate evidence of expertise
- Listen carefully
- Elicit patient input
- Offer limited options
- Prescribe a course of action

Placebo Effect of “Diagnosis”

GENERIC SYMPTOMS: BENEFITS OF DIAGNOSIS ALONE



D. Psychoeducational Counseling

- Name(s) of medication(s)
- Rationale for medication(s)' use
- When to take them
- What to do about missed doses
- How to tell if medications are working
- Lifestyle modifications during treatment
- Common side effects and rare serious side effects
- Expected duration of treatment
- How eventually to discontinue medication

RCT1: Psychoeducational Counseling and Reminders of Treatment Plan

- Hypothesis: Drug Counseling and/or treatment leaflet would increase antidepressant adherence and improve clinical outcome in **acutely depressed** primary care patients
- Setting: Primary care
- Subjects: 213 non-suicidal, clinically depressed outpatients

RCT1: Psychoeducational Counseling and Reminders of Treatment Plan

- “Treatment as usual”: Not described
- Intervention:
 - Informational leaflet with information on drug, unwanted effects, what to do after missing a dose
 - Counseling at weeks 2 and 8 by nurse focusing on:
 - lifestyle
 - attitudes to treatment
 - understanding reasons for treatment
 - education about depression and resources
 - importance of adherence

RCT1: Psychoeducational Counseling and Reminders of Treatment Plan

- Effects of Intervention:
 - **Counseling significantly increased adherence:**
Counseling had significant positive effect on clinical outcome (SF36 MH Subscale) in patients with major depression and at least 75 mg/d of designated antidepressant (dothiepin or amitriptyline)
 - **Leaflet did not increase adherence**

RCT2: Psychoeducation, Reminders, and a Written Treatment Plan

- Hypothesis: **Relapse prevention** intervention would improve continuation and maintenance phase adherence in patients with chronic depression
- Setting: Primary care
- Subjects: 386 non substance-abusing adults with
 - <4 DSMIV major depressive symptoms
 - ≥ 3 episodes of major depressive disorder or dysthymia

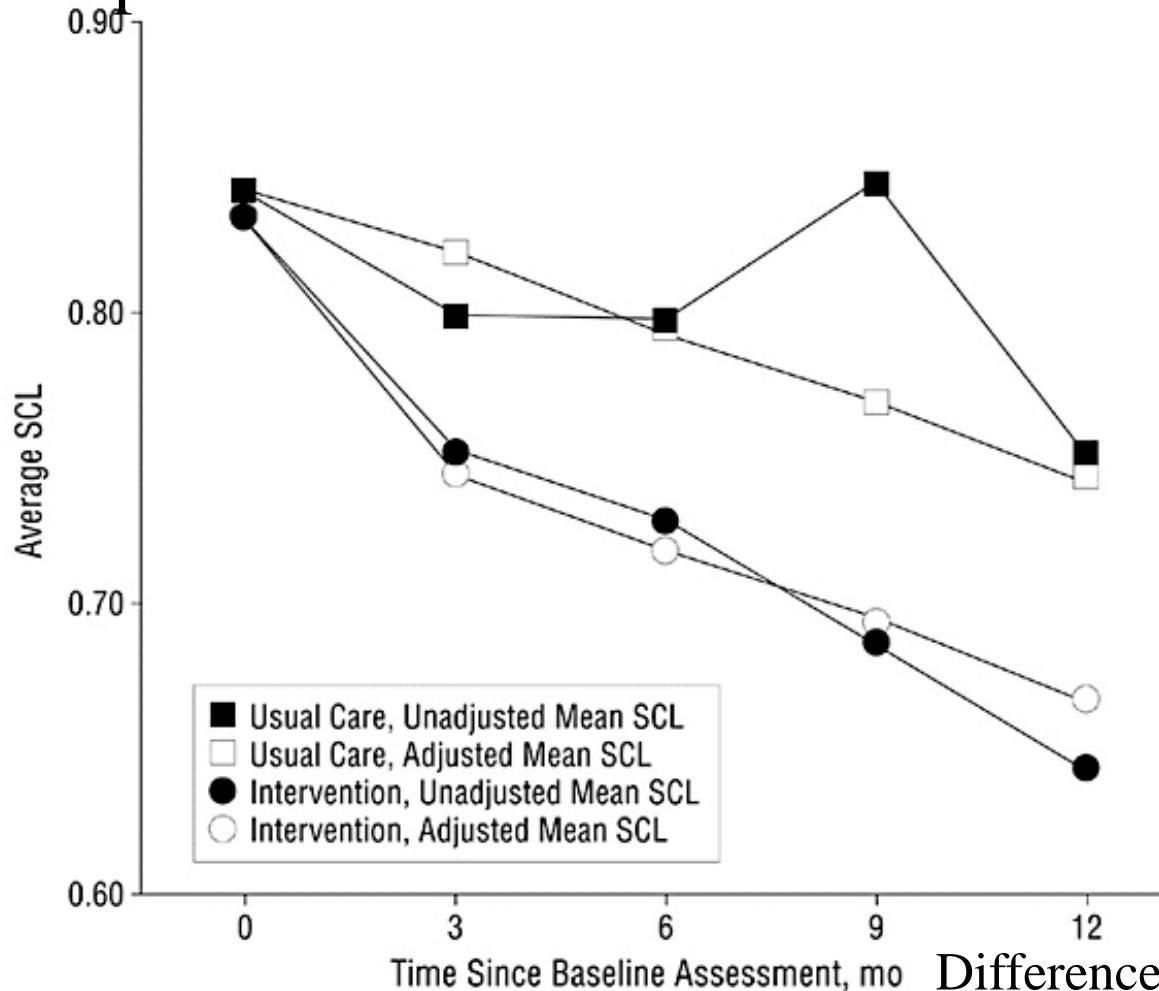
RCT2: Psychoeducation, Reminders, and a Written Treatment Plan

- Usual Care: 2-4 visits over 6 months
- Intervention:
 - Book & video tape, 2 primary care visits with depression specialist, 3 phone visits, and 4 personalized mailings over 1 year period emphasizing:
 - Adherence to antidepressant regimen
 - Recognition and monitoring of prodromal symptoms
 - Development of written relapse prevention plan
 - Clinician contact when refills missed or prodromal symptoms noted by patient on mailed checklist

RCT2: Psychoeducation, Reminders, and a Written Treatment Plan

- Effects of Intervention:
 - Decrease in depressive symptoms
 - Increased adherence to adequate antidepressant dosage (63.2% vs 49.7% at 12 months)
 - Likelihood of refilling prescription in 12 mo follow up period
 - No decrease in episodes of relapse/recurrence

SCL-20 Scores During 12-Month Relapse Prevention Intervention vs. Usual Care



Difference between I and UC significant at $p < 0.04$

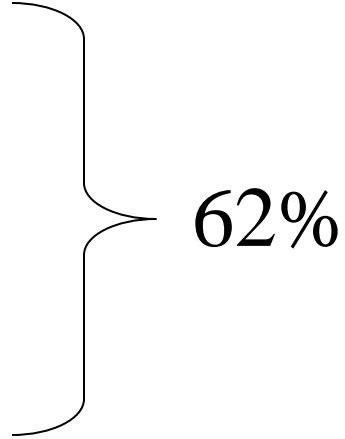
E. Monitor the Alliance

Transference to pharmacotherapist can be:

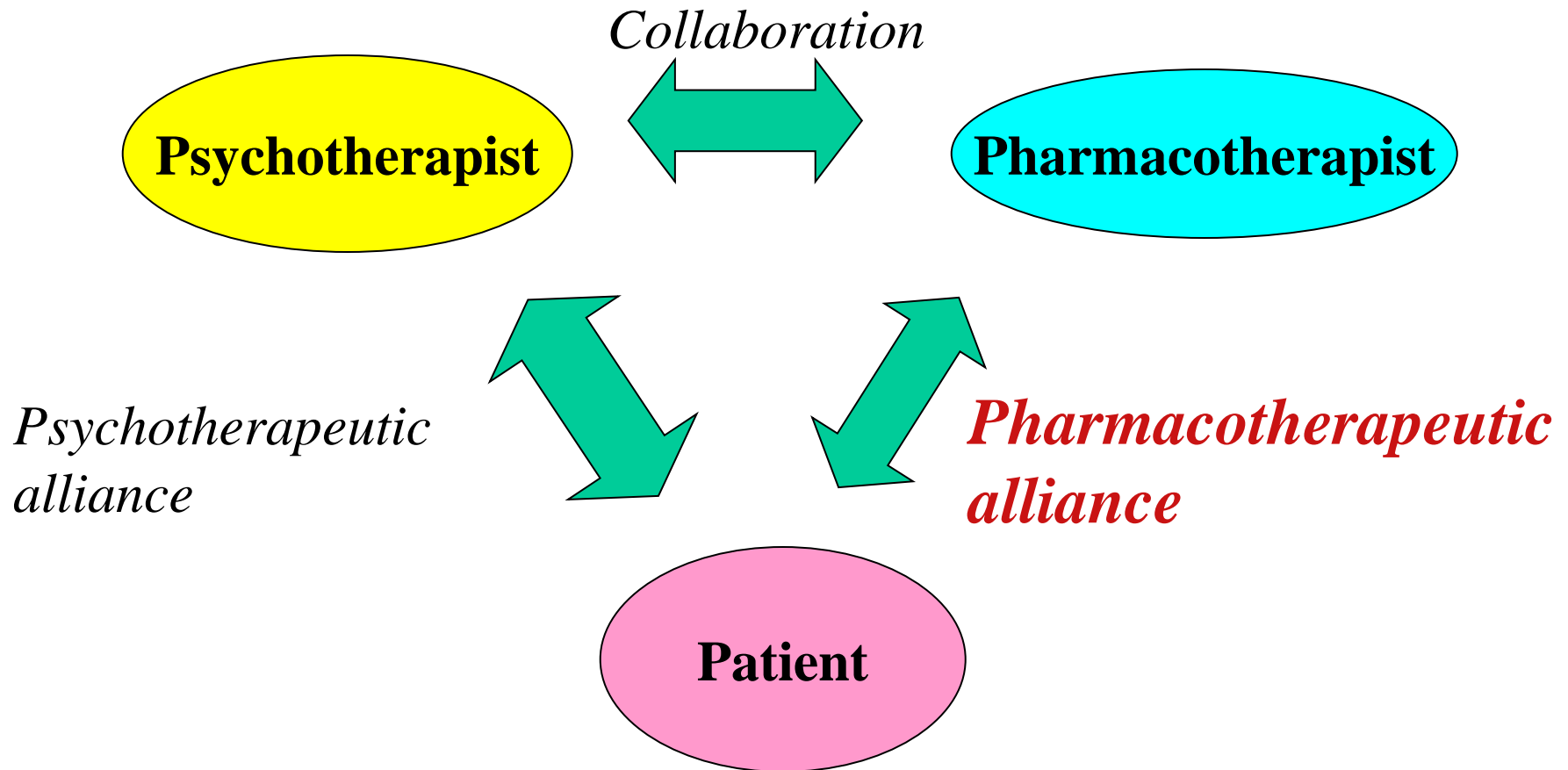
- Benevolently powerful –magical healer/nurturer
- Humane and helpful – concerned and caring
- Benign – a qualified and available technician
- Poor quality – but a forced choice
- Malevolently powerful – a controller, addicter, or poisoner

A frequent concern: *Treatment with medication implies devaluation of a person's uniqueness, of the psychosocial aspects of an illness, and of the person's own agency in recovery.*

Countertransference: Physicians' Reported Responses to Treatment Nonadherence

- Medical threat
 - Authoritarian tactics
 - Blaming/criticizing/insulting
 - Withdrawal
 - Task-oriented response
 - Trying to determine cause
 - Altering the regimen
- 
- 62%

F. In Collaborative Treatment, include other members of treatment team in alliance



Adapted from Ellison JM, Harney PA: Treatment-resistant depression and the collaborative treatment relationship. *J Psychotherapy Practice & Research* 2000;9:7-17.

Communication Tips (1): Referral Conversation

- Assess context and circumstances of request
- Obtain consent of patient for communication
- Share credentials and experience
- Discuss treatment philosophy

Communication Tips (2): Post-Assessment Discussion

- Case formulation
- Treatment approach and goals
- Implementation plans
- Mechanics of communication
 - Accessibility
 - Delineation of responsibility
 - Planning for emergencies
 - Agreement about subsequent communication

Communication Tips (3): Collaborative Relationship Maintenance

- Don't undermine or idealize treatment/clinician
- Maintain respectful communication as needed
- Address conflict early
- Use consultant when appropriate
- Dissolve collaboration, without abandonment, when necessary
- Patient care is first priority

G. Resist erosion and narrowing of the psychiatrist's treatment role

- Role/professional identity is increasingly determined by extrinsic factors
- Role satisfaction suffers with narrowing of scope of activity
- “Cost effectiveness” argument is used to support specialized use of psychiatrists and treatment disaggregation

Study 1: Are Psychiatrists Cost Effective Providing Combined Psychotherapy/Meds?

- Method:
 - Seven insurers' fee schedules from 1999 were used
 - Several clinical scenarios were compared for cost
 - 1) Combined treatment
 - 15 T* + 10 M*, 10 T + 5 M, 5 T + 3 M
 - Psychotherapy provided by psychiatrist, psychologist, social worker
 - 2) Medication management: 10 M, 5 M, 3 M
 - 3) Psychotherapy alone: 15 T, 10 T, 5 T

Dewan M: Am J Psychiatry. 1999;156:324-6.

(*T = covered psychotherapy session, M= covered medication session)

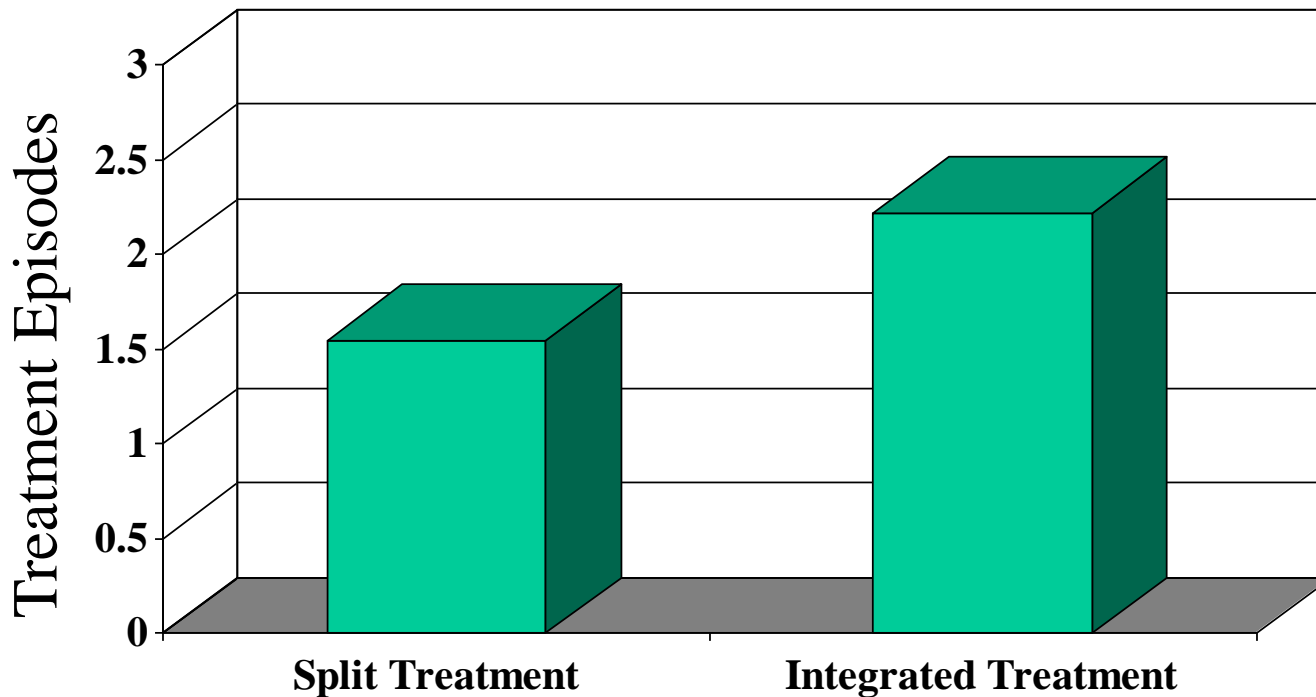
Study 1: Are Psychiatrists Cost Effective?

- Results:
 - Medication management alone was least costly.
 - Psychotherapy by MSW cost less than PhD, which cost less than psychotherapy by MD.
 - For patients in combined treatment, psychiatrist providing both modalities cost significantly less than MD/PhD split, a little less than MD/MSW split.

Study 2: Is Integrated Treatment More Cost Effective than Split Treatment?

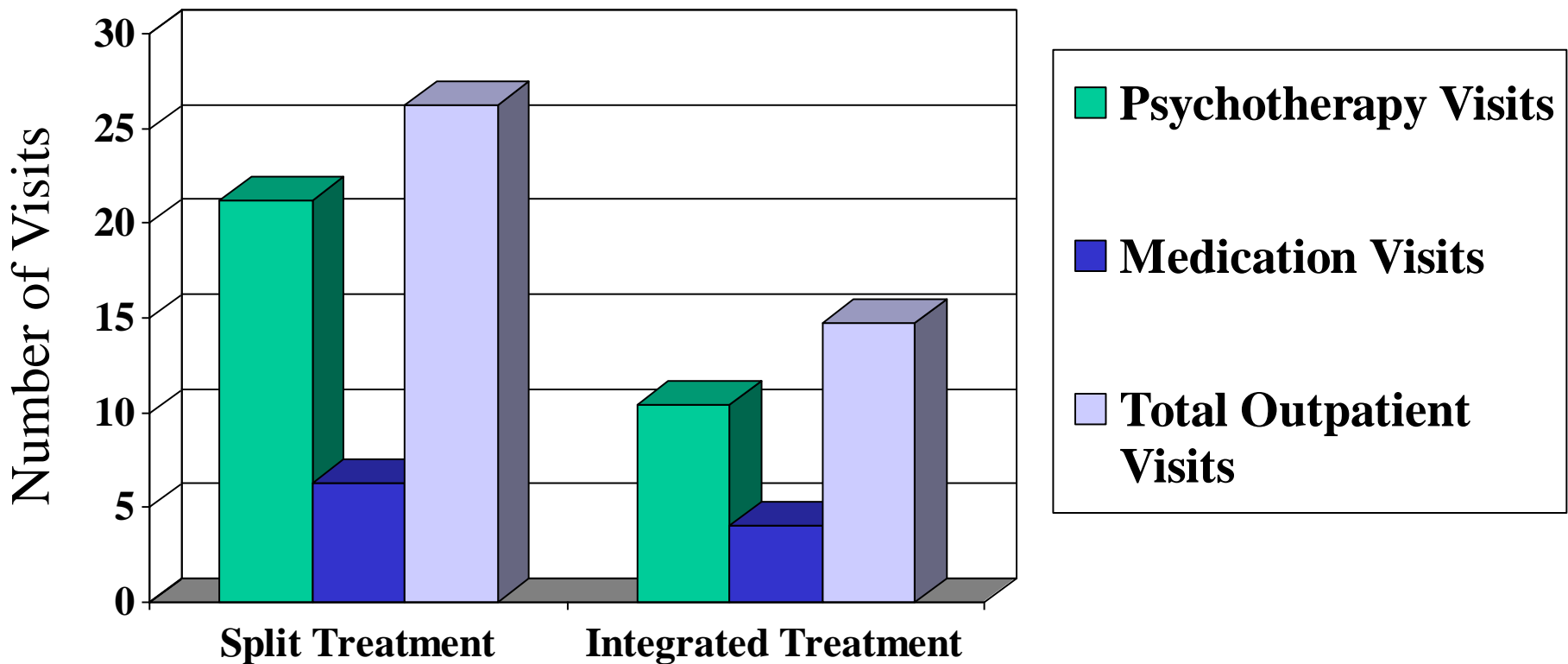
- Methodology of Goldman et al:
 - Retrospective comparison of claims data for 18 month period
 - USBH (managed mental health organization)
 - Compared patients in integrated vs. split treatment
 - Diagnoses:
 - Major depression
 - Dysthymic Disorder
 - Depressive Disorder NOS
 - Mood Disorder NOS

Integrated Treatment Occurred in More Episodes



P < 0.001

But Total Number of Visits Was Less with Integrated Treatment



P < 0.001

Conclusion: Integrated treatment costs less because it is more efficient

- Fewer total visits occurred during study period.
- Split treatment lacks efficient coordination of treatment modalities.
- Medication is initiated earlier in integrated treatment, preventing inefficient delays.
- Sessions spaced further apart makes for greater efficiency in use of services provided.

Conclusions

- Adherence is an important element of treatment success in depression.
- Multiple factors including the therapeutic alliance affect adherence.
- The therapeutic alliance can be improved by:
 - Creating an unhurried but efficient atmosphere
 - Listening actively to identify patient requests/needs
 - Harnessing the placebo effect
 - Providing psychoeducational counseling
 - Monitoring the treatment alliance
 - Including collaborative treaters in alliance
 - Resisting erosion/narrowing of psychiatrist's role

Self-Assessment Question #1

Which of the following is true?

- A. Thirty per cent or more of patients discontinue antidepressants during the first month of treatment.
- B. Adherence refers to the stickiness of a pill placed in the patient's mouth.
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Answer = A

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Which of the following is true of brief (5 to 10 minute) medication visits?

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- C. Meeting for only a few minutes in order to avoid nurturing a powerful transference
- D. Refraining from communication with other clinicians - whom the patient sees improves treatment adherence.

Answer = C

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Which of the following is true of the prescribing psychiatrist or nurse whose scope of activity is restricted to prescribing?

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- C. Splitting of treatment roles between a prescribing clinician and a psychotherapist may not always be cost-reducing.
- D. All of the above are true.

Answer = C

Citations:

- Berndt ER, Frank RG, McGuire TG: Alternative insurance arrangements and the treatment of depression: what are the facts? *Am J Manag Care* 1997;3:243-50.
- Blazer DG, Kessler RC, McGonagle KA, et al: The prevalence and distribution of major depression in a national community sample: the national comorbidity survey. *American Journal of Psychiatry* 1994;151:979-986.
- Brown WA: The placebo effect. *Scientific American*, January 1998:90-95.
- Bull SA, Hunkeler EM, Lee JY, et al. Discontinuing or switching selective serotonin-reuptake inhibitors. *Ann Pharmacother*. 2002;36(4):578-84.
- Dewan M: Are psychiatrists cost-effective? An analysis of integrated versus split treatment. *Am J Psychiatry*. 1999;156:324-6.
- DiMatteo MR, Sherbourne CD, Hays RD, et al: Physicians' characteristics influence patients' adherence to medical treatment: Results from the medical outcomes study. *Health Psychology* 1993;12:93-102.
- Ellison JM: Enhancing adherence in the pharmacotherapy relationship. In: Tasman A, Riba MB, Silk KR (eds): *The Doctor-Patient Relationship in Pharmacotherapy*. New York, The Guilford Press, 2000, pp. 71-94.
- Ellison JM, Harney PA: Treatment-resistant depression and the collaborative treatment relationship. *J Psychotherapy Practice & Research* 2000;9:7-17.
- Goldman W, McCulloch J, Cuffel B, et al: Outpatient utilization patterns of integrated and split psychotherapy and pharmacotherapy for depression. *Psychiatr Serv* 1998;49:477-82.
- Gutheil TG: Drug therapy: alliance and compliance. *Psychosomatics* 1978;19:219-25.
- Haynes RB, McDonald H, Garg AX, et al: Interventions for helping patients to follow prescriptions for medications. *The Cochrane Database of Systematic Reviews* 2002 (4).
- Haynes RB, McDonald HP, Garg AX: Helping patients follow prescribed treatment. *JAMA* 2002;288:2880-2883.
- Heszen-Klemens I: Patients' noncompliance and how doctors manage this. *Soc Sci Med* 1987;24:409-16.

Katon W, Rutter C, Ludman E, et al: A randomized trial of relapse prevention of depression in primary care. *Arch Gen Psychiatry* 2001;58:241-7.

Khan A, Brown WA: The placebo enigma in antidepressant clinical trials. *Journal of Clinical Psychopharmacology* 2001;21:123-5.

Korsch BM, Harding C: *The Intelligent Patient's Guide to the Doctor-Patient Relationship*. New York, Oxford University Press, 1997.

Krupnick JL, Sotsky SM, Simmens S, et al: The role of the therapeutic alliance in psychotherapy and pharmacotherapy outcome: treatment in the National Institute of Mental Health Treatment of Depression Collaborative research program. *J Consult Clin Psychol* 1996;64:532-9.

Lamberg L: Patient-physician relationship critical even during brief "medication checks". *JAMA* 2000;284:29-31.

Langewitz W, Denz M, Keller A, et al: Spontaneous talking time at start of consultation in outpatient clinic: cohort study. *British Medical Journal* 2002;325:682-3.

McDonald HP, Garg AX, Yayne RB: Interventions to enhance patient adherence to medication prescriptions. *JAMA* 2002;288:2868-2879.

Myers ED, Branthwaite A: Out-patient compliance with antidepressant medication. *Br J Psychiatry* 1992;160:83-6.

O'Brien MK, Petrie K, Raeburn J: Adherence to medication regimens: updating a complex medical issue. *Med Care Rev* 1992;49:435-54.

Olfson M, Marcus S, Druss B, et al: National trends in the outpatient treatment of depression. *JAMA* 2002;287:203-9.

Peveler R, George C, Kinmonth A-L, et al: Effect of antidepressant drug counselling and information leaflets on adherence to drug treatment in primary care: randomised controlled trial. *British Medical Journal* 1999;319:612-5.

Stimmel GL: Maximizing treatment outcome in depression: Strategies to overcome social stigma and noncompliance. *Disease Management & Health Outcomes* 2001;9:179-86.

Stimmel GL, McCombs JS, Aiso JY: Psychotropic drug-use patterns: Reality versus ideal. *TEN* 2001;3:66-8.

Vick S, Scott A: Agency in health care. Examining patients' preferences for attributes of the doctor-patient relationship. *J Health Economics* 1998;17:587-605.

Von Korff M, Katon W, Bush T, et al: Treatment costs, cost offset, and cost-effectiveness of collaborative management of depression. *Psychosom Med* 1998;60:143-9.

Zisook S, Hammond R, Jaffe K, et al: Outpatient requests, initial sessions and attrition. *Int J Psychiatry and Medicine* 1978-9;9:339-50.

The End