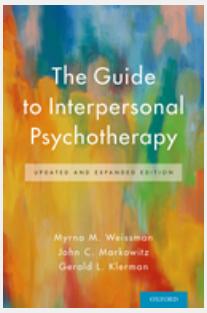

The Guide to Interpersonal Psychotherapy: Updated and Expanded Edition

Myrna M. Weissman, John C. Markowitz, and Gerald L. Klerman

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Beginning IPT

Chapter: (p. 30) Beginning IPT

Author(s): Myrna M. Weissman, John C. Markowitz, and Gerald L. Klerman

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This chapter describes the technical aspects of how to begin IPT, including how to assess depression and complete the tasks of the first sessions. Clinicians who are experienced in assessing depression can skip this section. We first describe the tasks of the opening sessions and explain how to carry them out. The order may vary slightly depending on the patient's clinical presentation, but by the end of the first phase, as the therapist, you should ensure that every task has been covered. You should strive to keep the initial phase of IPT brief, seeking to reach the middle phase as soon as possible.

Tasks of the Initial Visits

During the first three (or, if possible, fewer) visits, the IPT therapist takes a clinical history, collecting information about the patient's symptoms and current interpersonal situation. This allows you to make a psychiatric diagnosis and to select an interpersonal focus for the treatment. If the patient has not had a recent physical examination, especially if the patient is over the age of 50, recommend one to rule out physical explanations for depressive symptoms (e.g., hypothyroidism).

During the first visits the therapist:

1. Reviews the depressive symptoms and makes a diagnosis
2. Explains depression as a medical illness and describes the various treatment options
3. Evaluates the need for medication
4. Reviews the patient's current interpersonal world (the "interpersonal inventory") in order to diagnose the context in which the depression has arisen
5. Presents a formulation, linking the patient's illness to an interpersonal focus
6. Makes a treatment contract based on the formulation, and explains what to expect in treatment (p. 31)
7. Defines the framework and structure of treatment, including a time limit
8. Gives the patient the "sick role."

Review the Symptoms and Make the Diagnosis

Numerous scales have been developed to measure depressive symptoms (Rush et al., 2007). Among them, the Hamilton Rating Scale for Depression (Ham-D; Hamilton, 1960; see Appendix A) is a clinician-administered scale that has been used the longest and most widely, including in most studies of IPT. Many clinics now use self-report paper-and-pencil or computerized scales such as the Beck Depression Inventory (Beck, 1978) or PHQ-9 (Kroenke et al., 2001) in initial patient screening. The Ham-D does not diagnose depression but is a useful guide to help determine the specific symptoms and degree of suffering that depressed patients experience.

The Ham-D assesses symptoms that patients have experienced over the course of the previous week. In general, a total Ham-D score of 7 or less is considered normal, not depressed. A score of 9 to 12 indicates mild depression, usually not reaching the threshold of major depressive disorder (MDD). A score of 13 to 19 is consistent with moderate depression. A score of 20 or more indicates moderate to severe depression. A score of 30 or higher is clearly severe depression.

Antidepressant medication is likely to be helpful for any elevation in depressive symptoms, but patients with scores in the high 20s or in the 30s may require medication as part of their treatment in order to ensure an optimal outcome. This is not to say that IPT will not benefit patients with such high scores, but combined treatment may be preferable to monotherapy.

Whatever scale you use, plan to repeatedly administer it to your depressed patients over the course of IPT. Showing the patient symptoms on a standardized scale helps her to realize that what often feels like something personally bad and toxic is in fact a long-defined syndrome: the Hamilton scale has been around longer than many of the patients you may use it with. These outside sources thus contribute to psychoeducation and to making the disorder discrete and ego-alien. Repeating the scale periodically helps you and the patient to measure the progress of treatment. Simply seeing the symptoms listed on a scale may help to convince the patient that they are symptoms, not personal flaws. The frequency with which you repeat the scale is less important than doing it regularly: for example, every three or four weeks until the patient reaches remission (Ham-D < 8).

We recommend using the DSM-5 (American Psychiatric Association, 2013) or ICD-10 criteria to formally diagnose major depression, again giving the patient the opportunity to distinguish disorder from self. Emphasize that this is a treatable condition that is not the patient's fault. Table 4.1 lists the DSM-5 criteria for major depression.

Table 4.1 DSM-5 Criteria for Major Depression

American Psychiatric Association Diagnostic Criteria (DSM-5) for Major Depression

A. At least five of the following symptoms are present during the same two-week period nearly every day. At least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

1. Depressed mood most of the day, nearly every day
2. Diminished interest or pleasure in all or almost all activities, most of the day
3. Significant weight loss or weight gain when not dieting, or decrease or increase in appetite
4. Insomnia or hypersomnia (oversleeping) nearly every day
5. Psychomotor agitation or retardation nearly every day (observable by others)
6. Fatigue or loss of energy
7. Feeling of worthlessness or excessive or inappropriate guilt
8. Diminished ability to think, concentrate, or make a decision
9. Recurrent thoughts of death or suicide, a suicide attempt, or a specific plan for committing suicide

B. The symptoms cause clinically significant distress or impairment.
C. The episode is not attributable to the physiological effects of a substance or to another medical condition.
D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.
E. There has never been a manic episode or a hypomanic episode.

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Anxiety, Alcohol, Drugs

It is important to assess substance use as a potential confound or comorbidity compounding depression. Ask patients about the frequency and severity of alcohol use and the presence of related symptoms (hangovers, blackouts, seizures) and other drug use.

Explain the Diagnosis and Treatment Options

Once you have established that the patient has MDD, explain to the patient what depression is. While recognizing the patient's suffering, be clinically optimistic about the future. You might say something like:

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> *I understand that you're feeling awful. Depression is a treatable illness, and your chances of getting better are very good. You've said that you're feeling hopeless, but that hopelessness is a symptom of depression, not your true prognosis.*

Your clinical hopefulness does not mean that you should discount the patient's current suffering. It is also important to explain to the patient any comorbid diagnosis and how this may influence treatment.

We suggest that you first explain which of the patient's symptoms are part of the depressive diagnosis (e.g., sleep, guilt). Then educate the patient about depression in general:

> *Depression is a common disorder. It affects 3 to 4 percent of adults at any one time. Depression may feel like a hopeless condition, but that hopelessness is a symptom of the depression—it's not your prognosis. Even though you are suffering now, depression does respond to treatment. The outlook for your recovery with treatment is excellent. There are many effective treatments available—many different medications and different psychotherapies—so you do not need to feel pessimistic even if the first one does not work.*
>
> *Most people with depression recover quickly with treatment, and some even recover without treatment, although that may take longer. The prognosis is good, even though some people may need continuing treatment for extended periods in order to prevent recurrence. Once you receive treatment, you should return to normal functioning when the symptoms disappear.*

Therapist Note

Dysthymic, chronically depressed patients may actually improve with treatment to better functioning than what they have for too long considered "normal."

> *While you are depressed you may not feel like socializing or doing things that you usually do. You may need to explain this to your family members. However, you are going to be actively engaged in treatment and will be working hard toward recovery. The expectation is that, as you recover, you will resume your normal activities and should get back to normal, if not better. In fact, there is every reason to hope that you will be better than before, although it may be hard to believe this now, when you're feeling down and helpless and hopeless.*

The underlying message is that depression is a disorder over which the patient does not have full control, but from which the patient is likely to recover without serious residual damage. Treatment will hasten recovery.

(p. 34) Depression is *not* a failure, a punishment for past misconduct, or even a deliberate act. It is not something the patient has willed. In fact, it is important to emphasize that:

- Depression is a treatable medical illness.
- Depression is not the patient's fault.
- No one wants or tries to be depressed.

With many patients, it may be useful to recognize that suffering from depression represents a kind of vulnerability, in the same way that having diabetes or hypertension represents other types of vulnerability.

Evaluate the Need for Medication

Although an extensive literature supports the use of medication and psychotherapy alone and in combination in the treatment of depression (Cuijpers et al., 2013; Karyotaki et al., 2016), empirical studies have not determined when one approach will be superior to another for an individual patient. The recommendation of medication for a particular patient generally depends on the severity of symptoms, the patient's preference, the history of treatment response, and medical contraindication. If the patient has severe sleep and appetite disturbance, agitation, retardation, loss of interest in life, difficulty in thinking coherently; if there are no medical contraindications; and if the burden of depressive symptoms is severe, medication should probably be recommended, either alone or in combination with psychotherapy. As medication tends to work faster than psychotherapy, high suicide risk is a particular indication for medication—in addition to psychotherapy—for depressed patients. Indeed, high suicide risk may indicate the need for combined psychotherapy and pharmacotherapy. Pregnancy and lactation may be relative contraindications for medication. If you are not a physician, consider consulting with a psychiatrist about the need for medication with a depressed patient.

The presence of a life stress that brought on the depression does not preclude the use of medication, either with or without psychotherapy. If the patient is already taking medication but depressive symptoms persist, IPT can be added as an augmentation strategy. Because IPT and pharmacotherapy share a medical model of depression as an illness with both biological and environmental features, IPT is neatly compatible with antidepressant medication.

Review the Patient's Current Problems in Relationship to Depression (Interpersonal Inventory)

Once you have determined that your patient has clinical depression, explore what is going on in the patient's current social and family life that may be associated (p. 35) with the onset of the symptoms. In preparation for the subsequent sessions of IPT, you and the patient will choose one (or at most two) focal interpersonal problem areas to work on. The choices, again, are *grief, role dispute, role transition*, or *interpersonal deficits.* Choosing a problem area helps you and the patient to focus the therapy on the depression and the events surrounding it, rather than digressing into unstructured discussion on any topic that might surface.

Review who the *key people* are in the patient's life to get a full picture of her interpersonal connections. Explore the quality of important relationships:

- How close to people does the patient get? Can she confide intimate feelings and express needs or disagreements?
- To whom can the patient turn for support (even if she has withdrawn and is not using social supports at present)?
- Does the patient express anger when another person bothers her ("I don't like it when you …")? How effectively? How much comfort does the patient have in expressing her wishes ("I want …") and needs? These are typically difficult maneuvers for depressed patients.
- What beneficial and maladaptive patterns can you find in the patient's interactions with important others?

There are different ways to obtain this information, but the goal is to define the current primary problems temporally and emotionally related to the onset or maintenance of depressive symptoms. When reviewing important ties that may have relevance to the patient's symptoms,

keep a broad perspective. Consider the family, roommates, friends, coworkers, and other members of the social circle (Weissman, 2016).

It is useful to begin with a review. Some of the following questions may be helpful:

> *What was going on in your life and what was happening around the time you started feeling bad—at work, at home, with your family and friends? Had anything changed?*

It is best to leave these questions open-ended. Some withdrawn patients may require more specific prompting:

> *When you started to feel depressed, what was happening in your life? Was there a disappointment in a relationship? Did your marriage begin to have problems? Were you and your children or parents in a dispute? Did your child leave home? Did you start a new job? Did someone move in with you? Did you yourself move? Was it the anniversary of someone's death? Were you put in situations where you had to meet new people and establish relationships?*

Such life circumstances are often associated with depression. Try to determine—and help the patient try to understand—what might have triggered the onset of this (p. 36) depressive episode. Even if you can find no precipitant for the depressive episode, upsetting life situations are likely to emerge as consequences of the depressive episode itself. Strains in relationships (role disputes) and life changes—such as ending a relationship or job (role transitions)—may follow the onset of depressive symptoms. These still qualify as possible focal areas for IPT, inasmuch as IPT focuses on the connection between one's life situation and mood rather than causality.

Asking these questions may help you to find a social and an interpersonal context for the patient's depression. Your aim will be to link the patient's interpersonal situation (a spouse's affair, a mother's death, a move to a different city) to the onset of symptoms in a brief contextualizing narrative that makes sense to both the patient and you. Patient self-report forms have been developed to assess problem areas (Weissman, 2005).

The problem areas on which IPT therapists focus treatment fall into four groups, as listed in Table 4.2.

Table 4.2 IPT Problem Areas

Problem Area	**Life Situation**
Grief	*Complicated bereavement* following the death of a significant other or close relative (Chapter 5)
Role dispute	*Struggle*, disagreement with spouse, lover, child, other family member, friend, or coworker (Chapter 6)
Role transition	*Life change*: graduation, a new job, leaving one's family, divorce, going away to school, a move, a new home, retirement, medical illness, immigration (Chapter 7)

Interpersonal deficits	*No acute life events*: none of the above. Paucity of attachments, loneliness, social isolation, boredom. (This category does not necessarily mean the patient has a personality disorder.) (Chapter 8)

Obviously these problem areas are not mutually exclusive, and you may find that what the patient thought was the central problem is merely the tip of an iceberg. Use the initial sessions to ensure that you have focused on a pivotal, emotionally meaningful area for the patient and that you have ruled out surprises that might otherwise arise later in treatment. Choosing a good focus is essential to an organized and focused therapy for patients whose depression may cause disorganization, distractibility, and poor concentration.

Most depressed people have more than one interpersonal problem area. For the purpose of organizing the therapy and helping to treat a major depressive episode, however, you should focus on one (or at most two) during the course of the treatment. One is preferable. To choose multiple foci risks diluting the treatment so that there is no real focus at all. We recognize that selecting only one is not always easy, especially for clinicians without prior experience in time-limited therapies. However, our experience is that, with some practice, most clinicians are able to correctly select the main focus. Research has found that IPT therapists agree in choosing a primary focus (Markowitz et al., 2000).

(p. 37) In working on complicated grief over the death of a loved one, you may help the patient to handle role disputes with other family members while still focusing the overall treatment on the grief. It is preferable to keep things simple, keeping sorrow as the overarching topic, rather than to give the patient a laundry list of interpersonal problems. Sometimes the patient's problems may change during the course of treatment (particularly, of course, in the maintenance phase). For example, a woman who comes in saying, "My children are my big problem" may later, as she gets to know you, bring up the more pressing area of distress: her spouse's extramarital affair. (Again, it is best to try to uncover this at the start.) The idea is to identify the most recent and most disturbing stresses at the outset.

Some patients initially concentrate on the physical symptoms of depression, such as sleep and appetite disturbance, because they feel these to be the most distressing. They may not believe that there is a connection between their life circumstances and these symptoms, or they may either secretly or openly fear having some undetected physical illness. Although this is often only a fear, depressive symptoms can appear in the context of a variety of physical illnesses, and depressive patients tend to neglect their physical health. Hence a physical examination often helps to clarify the diagnosis.

Tell the patient:

> *Over the next few weeks, we'll try to understand the interpersonal situation(s) that may be related to some of the symptoms that are making you uncomfortable. Solving those problems situations is likely to help you feel better.*

Present the Formulation

In the first few sessions, you need to establish the diagnosis of depression and identify the patient's interpersonal problems. Next, tie together the depressive diagnosis and its interpersonal context in a treatment formulation, providing a potential focus for the IPT treatment. A formulation might sound like this:

You've given me a lot of helpful information in the last two sessions. May I give you some feedback to see whether you think I understand your situation? . . . We've already established that you are suffering from an episode of major depression, which is reflected in your Hamilton Rating Scale for Depression score of 25. (As we've discussed, depression is a treatable illness and not your fault.) From what you've told me, your depression seems related to what has been going on in your life recently, namely:

- *The death of your mother, a terrible blow that you have had trouble adjusting to. We call this grief, or complicated bereavement. [or]*
- *Your struggle with your husband about whether to move/have another baby/give up your career. We call this a role dispute. [or]* (p. 38)
- *Your life has turned upside down since you moved/changed jobs/got married/got divorced/were diagnosed with leukemia. We call this a role transition. [or]*
- *Your social isolation, lack of friends, loneliness, or boredom. [To tell patients they have "interpersonal deficits" risks sounding insulting.]*

This kind of interpersonal situation has a proven association with depression. What causes depression is unknown, and it probably has multiple causes, but it is often related to life problems like the ones you've described.

I propose that, for the next X weeks, we focus on helping you solve your [complicated bereavement/role dispute/role transition/social isolation]. If you can solve that problem, not only will you improve your life situation, but your depressive symptoms are likely to improve as well. Repeated research studies have shown this to be the case. Does this plan make sense to you?

This formulation is a key juncture, the bridge between the initial phase and the rest of treatment, whose focus it determines. Choosing the focal point requires clinical acumen. Again, your goal is to choose a plausible, simple focus based on the patient's history, an organizing narrative to which the patient can relate and which helps the patient to feel understood (Markowitz & Swartz, 2006).

Present the formulation early in the therapy, no later than the third session, so that sufficient time remains for the middle and termination phases of treatment. The early, explicit formulation, which defines the focus for the rest of the treatment, is a powerful organizing feature of IPT.

Make the Treatment Contract and Explain What to Expect

Note that the formulation concludes with a proposed treatment contract. You ask whether the patient agrees with this formulation and is willing to work on it for the next X weeks. Practical and financial considerations determine the precise number of sessions to recommend (generally eight to sixteen weekly sessions). Predetermine a fixed number (e.g., twelve weeks), not a range, and aim to make these *consecutive* weekly sessions in order to maintain treatment momentum. An important function of the time limit is to pressure the patient (as well as the therapist), combatting depressive passivity and moving the therapy forward. Thus, more sessions are not necessarily more helpful.

Your presentation of the formulation thus constitutes a treatment contract. You may use this opportunity to explain again the relationship that often occurs between symptoms and problems in life. The patient's agreement on this focus seals the contract. You need to obtain an explicit agreement on this crucial point. Thereafter, if the patient should digress from the focus, you can bring the treatment back to this agreed-upon theme. This treatment focus should be seen as a

(p. 39) collaborative effort. Although patients usually accept the presented focus, if the patient disagrees with it, you should explore what the patient sees as an alternative interpersonal focus and might well agree to pursue that.

The Sick Role

Another facet of the initial phase of IPT is to give your patients the "sick role," excusing them from blame for the depression and for what the depression prevents them from being able to do. You can often helpfully make analogies to other medical illnesses:

> *No one is at her best when suffering from an illness. If you had appendicitis or the flu, you wouldn't blame yourself for being unable to perform at your best. Depression is no different, in some ways even worse.*
>
> *The symptoms of depression may prevent you from dealing with other people as successfully as usual. We will try to discover what you want and need from others and learn what options you have and how to get them. We will also talk about what options are unrealistic and not possible. This is a good time to experiment with handling situations: we can discuss afterward what's gone right or gone badly. On the other hand, if you can't do certain things because you're feeling too depressed or exhausted or hopeless, that's too bad (we'd like to see how you handle such situations), but don't beat yourself up—you're not to blame for being ill. We expect that over the course of treatment you will regain the ability to do all of those things. You're fighting an illness, but it's a treatable illness.*

After giving the patient an initial understanding of how you see the problem and agreeing on the focus of treatment, emphasize the following:

- *We will be focusing on your life as it is now.*
- *Therapy will focus on your relationships with important people in your life.*
- *We will discuss these relationships and your feelings. If you feel that the direction of the sessions is not useful or that I'm doing something that's bothering you, please let me know. I won't be offended, and your feelings are important.*

Discuss the expected duration and frequency of the treatment, including how often you will be meeting. The usual time is once a week for about fifty minutes for a period of three to four months. Set a firm time limit, and hold to it so that both you and the patient have a timeline by which to measure progress. Depressed persons who recover from an episode but require maintenance treatment to prevent recurrence may subsequently contract to continue treatment for extended periods at a reduced session frequency.

(p. 40) A couple of additional things to mention to the patient:

- *Anything you tell me will be kept in confidence. The only exceptions are legal ones (like child abuse or your intending to harm or kill someone). Otherwise, I won't talk to anyone about our treatment without your permission.*
- *In the therapy we will discuss feelings and situations that concern you and may be related to your depression. I am interested not only in what happens to you in between sessions but also in your feelings about these events. You can select the topics that are the most important to you since you are the one who knows best what things bother you.*

Entering the Intermediate Sessions

Following the diagnosis, identification of the problem areas, agreement on the formulation, and establishment of the treatment contract, the work of IPT begins on the problem area: grief, interpersonal disputes, transitions, or (in the absence of any of the first three) interpersonal deficits.

Begin each session after the first one by reviewing the patient's last week. The archetypical opening question is:

> *How have things been since we last met?*

If the patient begins by discussing mood ("I've been feeling awful"), ask about the interpersonal context:

> *I'm sorry to hear that. Did anything happen this past week that might have contributed to your feeling that way?*

Conversely, if the patient answers the initial question by reporting an event ("I had a terrible day at work"; "It was my birthday Tuesday and I got drunk"), link it to mood:

> *Sorry to hear that. How did that make you feel?*

With two questions, then, you should be able to elicit a recent incident about which the patient has feelings. The next step is to explore the incident and the patient's feelings about it. What happened? How did the patient feel about what happened? What did the patient want or expect to happen? What were the specifics of the encounter? Try to recreate a transcript of the encounter, including the patient's actual words and tone of voice, her feelings as the interchange transpired, and the other person's reactions.

For example, if the patient reports a disagreement with a spouse, family member, or coworker, you would want to dissect the incident. At each juncture, ask:

> *What did you say then?*
>
> *How did [the other person] respond?*
>
> *Then how did you feel?*

(p. 41) By reconstructing such incidents, pulling for both the patient's feelings and behaviors in interpersonal situations, you gain a better understanding of how the patient's life is proceeding and how she is handling crucial encounters.

If the patient has handled such an event well and is feeling a little better, it is important to note the connection between capable interpersonal functioning and improved mood. Moreover, you want to reinforce adaptive functioning:

> *Great work! No wonder you're feeling a little better.*

If things have gone badly, as is more often the case early in treatment when the patient is most depressed, a similar but inverse approach applies: you want to help the patient understand the connection between bad events and worsening mood and depressive symptoms. Further, it is a

chance to examine what has gone wrong in the interpersonal setting and how the patient might handle a similar situation the next time it arises:

> *Well, that sounds painful. I'm sorry to hear about it. But let's try to figure out where things went wrong . . . That strategy doesn't seem to be working. What other options do you have? What could you do in that situation if (as is likely) it were to happen again?*

Listen for disjunctions—dissonances between the patient's feelings and actions. If the patient felt angry but said nothing, was the feeling of anger understandable and warranted, and did that silence contribute to an unsatisfactory encounter? It's important to validate the patient's feelings, particularly negative affects such as anger or sadness that depressed patients may see as bad or shameful. Yet if the patient dismisses such feelings as "bad" rather than understanding them as useful social information, she will probably not act on them, and the encounter will likely leave her feeling worse. Your role is to help the patient recognize that negative affects are normal and useful (rather than bad) and are key to handling encounters with other people:

> *Everyone feels angry when someone is bothering them. That's how you know that they're bothering you.*

Having normalized these affects, what can the patient do with them? What other options might she have for handling such a situation? Depressed patients will frequently state that they have no options for managing a situation. Feeling hopeless, they will say they've "tried everything" or "nothing works." This is rarely true. The patient's previous efforts may have been half-hearted, and she may well have overlooked viable options because of discouragement, a sense that there was no reason to be upset by such a behavior, and so on. With some gentle questioning and encouragement, you can often get the patient to come up with feasible options. It is best to let the patient come up with the ideas, so that she feels **(p. 42)** competent and can take credit for the development, rather than suggesting them yourself (which makes you look good and the patient feel incompetent).

If someone is bothering a patient and she says nothing, feeling the resultant anger is just part of her problem, and this has negative interpersonal consequences. People expect other people to tell them when to back off. If the patient is silent when bothered, ignoring her reaction and trying to put other people's needs first, the other people may not even know they're bothering her—and are likely to keep repeating the offending behavior. Tolerating our negative feelings (anger, sadness, anxiety) and finding a way to verbalize them clarifies the situation, communicates interpersonal understanding, and generally relieves tension. The patient who can say, "Please don't do that. I don't like it when you do that," is likely to feel better and to find that she has greater control over her interpersonal environment.

But this takes practice. After exploring options and finding a new, potentially feasible strategy, you can then role play this with the patient:

> *What would you like to say to [that person]?*
>
> *How did [the way you just said] that sound to you? Did you say what you wanted to get across? What did you think about your tone of voice?*

Repeat the role play until the patient feels more comfortable with the intervention. The session usually ends with a summary of what has been covered and how it relates to the patient's depression.

This loosely structured sequence is the heart of the IPT intervention. The therapist focuses consistently on mood and interpersonal interaction, helping the patient to see the link between them, reinforcing adaptive interpersonal functioning, and helping the patient to explore and gain comfort with new options where old strategies have not been working. Given this emphasis in the therapy, it is hardly surprising that research has shown IPT helps patients to develop better psychosocial functioning.

Involvement of Others

Although IPT is usually conducted as an individual psychotherapy, you may ask other family members to participate in one or two sessions if you and the patient feel that it would be helpful. With adolescents or children (Chapter 14), parents are always invited to participate in the initial sessions. Involvement of family members also occurs in situations of family, husband–wife, and/or parent–child disputes that have come to an impasse (see Chapter 25 on conjoint therapy). In some cultures, family members expect to participate in multiple sessions (Chapter 24; Weissman, 2016).