

What We Know About Psychotherapies

Plain-Language Evidence Summaries for Mental Health Professionals, Patients and Policymakers

Pim Cuijpers with Mathias Harrer

METAPSY

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The texts in this booklet were first published as evidence summaries on metapsy.org.

This booklet summarises research findings. It does not replace advice from a clinician about your own situation.

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About this booklet

The texts in this booklet were first published as evidence summaries on the Metapsy website. In each of them, Pim Cuijpers tries to answer a question from patients and clinicians, based on what is known in science about psychological treatments. The knowledge is mostly drawn from the collective work of the Metapsy collaboration over at least 15 years.

About the authors

- Pim Cuijpers is professor emeritus of clinical psychology at the Vrije Universiteit Amsterdam and scientific director of Metapsy. He has been involved in more than 1,100 scientific studies, mostly on psychological treatments of mental health problems.
- Mathias Harrer is assistant professor at the Vrije Universiteit Amsterdam and the developer and maintainer of the Metapsy infrastructure.



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CHAPTER 1

Fundamentals

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1

Does psychotherapy work?

"I am not feeling well for quite a while now and my partner says I should get therapy. But I doubt about that because I am not sure if it works. Can therapy really help me?"

The short answer

The simple answer is yes, therapy works. However, that does not mean that everyone will be completely recovered after receiving therapy.

Many therapies, many conditions

There are many types of therapy that are indeed effective. Effective therapies exist for depression, generalized anxiety disorder, panic disorder, social anxiety disorder, post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), insomnia, health anxiety and many other mental health conditions. For each of these problems, different types of therapy have been developed and tested.

Cognitive behavior therapy is perhaps the best known type of therapy, but there are many other types of therapy, including for example psychodynamic therapies, exposure-based therapy, acceptance and commitment therapy and many more. It has been estimated that there are a few hundred different types of therapy.

Some of these therapies have been examined in well-designed scientific studies. In such studies, also called randomized controlled trials, people who received these therapies were compared to people who did not get these therapies. That is why we know that they are more effective than not getting therapy. Not all therapies have been tested well and for many therapies it is not known whether they work or not.

> *If you want to know if a specific type of therapy is effective in the treatment of mental health problems, you can go to the website of the Metapsy project. There you can find a summary of the effects of the best examined types of therapy for eight mental health conditions: metapsy.org/database/explore. This website gives information about the chance of getting better when you get a specific type of therapy and how trustworthy these outcomes are.*

Format matters less than you might think

Therapies are traditionally provided individually, meaning that the patient has individual sessions with a therapist. But therapies can also be provided in groups, by telephone or digitally through the internet.

There is no evidence that one of these treatment formats is more effective than others. Sessions can vary considerably between therapies and conditions, but often a therapy is between 6 and 24 sessions.

How often does it actually work?

Many people get better when they receive therapy, but certainly not everyone. On average the chance of improving (defined as a 50% symptom reduction) is for example:

- 42% for depression
- between 30 and 40% for anxiety disorders, PTSD and OCD
- 25% for borderline personality disorder

That means that many people have not recovered or substantially improved through therapy. When you are receiving treatment and do not get better, your therapist will probably discuss with you to extend the therapy, to start another type of therapy, or for example combine the therapy with medication. In the end most people who receive mental health treatment do get better, but often not after the first treatment.

> *So yes, therapy certainly works, but not right away for everyone.*

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2

Does therapy take away the causes of mental disorders?

"I am using antidepressants now for a while, and they have helped me quite a lot. I talked with a friend yesterday and she said that antidepressants do not take away the causes of depression, but that good therapy does take away these causes. Is that true? And should I stop using my medication and switch to therapy?"

The uncomfortable truth: we don't know the causes

Unfortunately, it is not known what the exact causes of depression are. It is known that people who have experienced serious life events (such as the loss of a loved one) or chronic stressors (such as caring for an ill partner) have a depression more often than other people. However, there are also many people who have had serious life events or chronic stressors who do not get a depression. Actually, the large majority of people with these experiences do not develop a depression. This means that such events are not sufficient for getting a depression. Maybe there is some kind of biological, psychological or social vulnerability, but there is not enough knowledge about such pathways leading to depression.

We know that treatments work, not how they work

It is also not known how antidepressants work or how psychotherapies work and whether therapies can actually take away the causes of depression. There are several theories on how treatments work, and some of these do have a limited amount of empirical support. But at this moment it is not possible to say how these treatments work.

> *There is clear evidence that these treatments work, but not how they work.*

That is related to the fact that the effects of treatments can be examined with the best scientific studies (randomized controlled trials), while such studies cannot be used to examine how they work.

So what should you do with your medication?

This means that we do not know what the exact causes of depression are and that we also do not know how therapies work. From that perspective it is not automatically the best solution to stop with antidepressants and to start with psychotherapy. But there are several considerations to take into account when you want to stop using antidepressants.

First of all, this should be discussed with your clinician. There may be reasons to stop with antidepressants, but this cannot be done on your own. Your clinician can give advice on that and help with the tapering of the medication.

It is also not necessary to stop with your medication before going into therapy. You can certainly do both. There is no reason whatsoever to assume that taking drugs reduces the effects of therapy. In fact, there is considerable evidence that the combination of medication and therapy is the most effective treatment and better than medication or therapy alone. That is true at the short and at the longer term.

What therapies actually focus on

Although there is not enough evidence on how therapies exactly work, they do focus on psychological factors that are related to depression. For example:

- In cognitive behavior therapy you learn how to identify, challenge and change negative or distorted thought patterns.
- In behavioral activation you learn to identify meaningful and enjoyable activities and to engage more in them.
- In interpersonal psychotherapy you learn how to improve interpersonal relationships.
- In brief psychodynamic therapy you can enhance your understanding, awareness and insight about repetitive conflicts.

If these are issues you struggle with and want to learn how to handle them, then psychotherapy is certainly a good choice, with or without medication.

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3

Is the therapeutic alliance the most important part of therapy?

"During my training as a therapist, I learned that a good alliance between therapist and patient is the most important change mechanism of psychotherapy. But in practice I also use very specific techniques that I see working in patients. So which one is true? Or can they both be helpful at the same time?"

A good relationship is essential by definition

There is no doubt that the relationship between a patient and a therapist is important. Therapy can be defined as something that happens in the relationship between patient and therapist. That means the quality of that relationship is, by definition, an essential part of the therapy. If the relationship is not good, then the therapy is also not good.

It is less clear, however, whether the alliance is what actually causes the change in patients. That is because very little is known about how therapies work.

> *We know that therapies work. We do not know how.*

Knowing that something works, but not how

To examine whether a therapy works, we can use a very strong scientific method: the randomized controlled trial. In such a study, a group of people with a mental health problem is split into two subgroups in a random way. One subgroup gets the treatment and the other does not, but otherwise the two groups are exactly the same. When the treatment ends and there are differences between the subgroups, these differences can logically only be caused by the treatment. This is the strongest design available in science to show that a therapy has caused change in a patient.

Examining how a therapy works is much more complicated, and the same strong research design cannot be used. Suppose that a therapy has been shown to be effective in reducing depression in a randomized trial, and we think that this may be caused by a reduction in negative thinking. We can look in the study at whether change in depression is associated with change in negative thinking. But even if

we find such an association, that does not mean that the change in depression is caused by the change in negative thinking. It is just as possible that the change in negative thinking is caused by the improvement in depression. Or that a third factor, for example the alliance, causes both. There is no way to say with certainty which of these three possibilities is true.

This means that we do not know how therapies work, and we do not know whether the change is caused by the alliance, by specific techniques, or by something else entirely.

This is not a problem unique to psychotherapy

Psychotherapies are not an exception. It is also not known how antidepressants work. Even outside of medicine, we still do not know exactly how smoking causes cancer. We know that it causes cancer, and we know some of the mechanisms involved, but the precise process by which smoke enters the lungs, affects the body and leads to cancer is also not fully understood.

> *Knowing that something works, and knowing the exact mechanism by which it works, are two very different questions.*

How researchers try to get a little more certainty

Even without a randomized trial of the mechanism itself, it is possible to gather evidence that makes one explanation more plausible than another. Researchers can examine, for example:

- Whether the change in the candidate mechanism (e.g. negative thinking) comes before the change in the outcome.
- Whether there is a dose-response association between the two: more change in the mechanism, more change in the outcome.
- Whether, among many variables measured in the same study, the candidate mechanism is the one most strongly associated with the outcome.
- Whether there is a clear theoretical framework explaining why specifically this factor should cause change.
- Whether laboratory or experimental studies support the association.

None of these elements on their own can prove causality, but together they can make a mechanism more or less likely.

So, what about the alliance?

There is much research showing that the alliance and positive outcomes are correlated. But as explained above, correlation is not enough to conclude that the alliance causes the change. There are also some studies showing that the alliance

is already developing before the change in outcomes appears, which supports the hypothesis that it is a causal mechanism.

> *Overall, however, the evidence is still not strong enough to conclude that the alliance is itself a causal factor.*

What this means for clinicians

What does this mean in practice? You should, of course, develop a good working relationship with every patient, because that is the core of what therapy is. The fact that science cannot say whether there is a causal association with the outcome does not change this in any way.

But it also means that you should apply the specific techniques of the therapy as well as possible, because these may also cause change. Assuming that both are essential is probably the best strategy.

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4

What makes randomized controlled trials the gold standard?

"As a clinician, I sometimes get tired of hearing that randomized controlled trials are the gold standard for examining outcomes. There are other types of research that are also important if we want to learn about the effects of therapies. Why should we pay so much more attention to randomized controlled trials?"

All research designs have value

There are many types of studies that can help us understand therapies and their effects—and they are all important. Qualitative research can give essential insight into patients' experiences and generate hypotheses about outcomes, mechanisms, and priorities for research. Studies that follow patients over time without a control group can tell us how many patients improve and by how much. Single-case studies provide unique insights into the processes patients go through during therapy and can reveal potential mechanisms that other designs cannot capture.

These studies—and many others—are essential if we want to understand how therapies work, how well they work, for whom, and how we can implement them in routine care. There is no simple hierarchy that says one type of research is "the best". Each design has its own strengths and limitations, and each is well-suited to specific kinds of research questions.

The one thing that sets RCTs apart

Randomized controlled trials (RCTs), however, have one characteristic that no other design shares: they can tell us whether a therapy caused an improvement—not just that improvement happened alongside therapy.

In an RCT, a group of people with a mental health problem is split into two subgroups at random. One subgroup receives the treatment; the other does not. Because the split is random, both groups end up—on average—identical in every other way: same distribution of age, same symptom severity, same proportion of men and women, same likelihood of having other health conditions. When the

treatment ends and differences between the two groups emerge, those differences can logically only have been caused by the treatment.

> *This is the power of randomization: it balances all known and unknown characteristics between groups—without the researcher needing to know in advance what those characteristics are.*

Why this matters for patients

In healthcare it matters enormously that we only offer treatments that have genuinely been shown to work. We do not want to give patients treatments that may be ineffective or even harmful—whether for physical or mental health conditions. And the most reliable way to demonstrate that a treatment works is through a randomized trial. No other study design can make the same claim with the same certainty.

This does not mean that RCTs are "more important" than other types of research—only that they are uniquely suited to the question of whether a therapy causes improvement.

Other designs come close—but not quite

Some study designs approximate the logic of RCTs. Observational studies using propensity score methods, for example, statistically control for a wide range of factors that could influence outcomes, bringing comparison groups closer together. Other designs take multiple measurements before and after an intervention, making it possible to detect whether a change occurred specifically during the treatment period.

But none of these approaches fully eliminates the possibility that some unmeasured factor—something the researcher did not think to control for—is responsible for the observed results. With true randomization, no such factor can systematically favor one group over the other.

RCTs have real limitations too

That said, RCTs are far from perfect. Many trials have some degree of risk of bias—methodological weaknesses that can undermine the confidence we place in their findings. They are also often conducted with carefully selected patient samples, which raises legitimate questions about how well the results translate to the full range of people seen in routine clinical care.

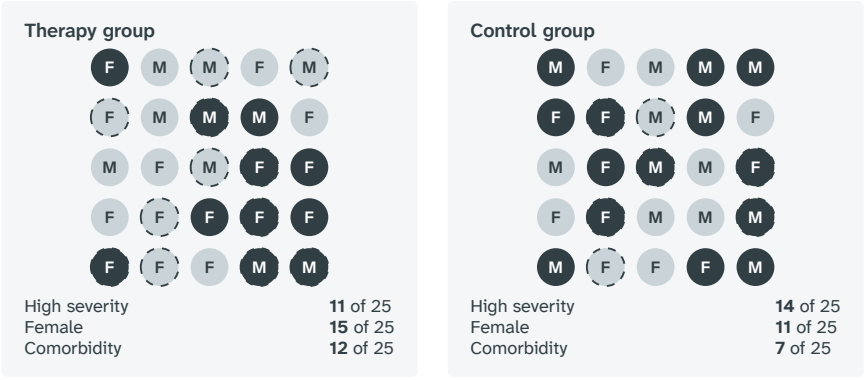
These are real limitations, and they are why the field works hard to improve how trials are designed and reported—and why systematic reviews and meta-analyses, which pool and critically evaluate evidence across many studies, are so valuable.

Randomization in action

50 patients, randomly assigned to two groups. Nobody chose who goes where, yet the groups end up (almost) balanced on severity, gender and comorbidity. This is one random draw; on the website you can try it yourself.

High symptom severity Low severity

F = female, M = male; dashed ring = has comorbidity



The bottom line

When we want to know whether a treatment works, there is no substitute for the randomized controlled trial. That does not diminish the value of other research designs—it simply recognizes that each design has its domain. For the specific question of whether a treatment causes improvement, the RCT stands alone.

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5

If we don't know what mental disorders are, how can we still treat them?

"I have read on the internet about depression and if I understand it well, it is basically unknown what a depression is. So if we don't know what depression is, is it still possible to treat it? How is that possible?"

We can see mental disorders, even if we can't define them perfectly

It is indeed still not clear what a depression (or any other mental disorder) exactly is. There are no blood tests or any other objective tests that can say whether someone has a depression. Of course we know that depression exists, because we can see people suffering from it. But we don't know what it is, or why one person gets it and another not in the same circumstances.

Basically, we say that someone has a depression when that person meets a number of criteria according to a list of criteria that was made by a group of experts, like in the classification systems of the DSM or ICD. But in reality it is not clear what the threshold is for having a depression or not. And it could be caused by a biological problem, a psychological problem, a social problem, or a combination of these. Science has still not established what the exact pathways are that cause depression.

You don't need to know the cause to know what helps

But we can develop effective treatments, even though we do not know what depression is. That is because we can use so-called randomized controlled trials to examine the effects of a treatment. In such a study a group of people with depression are split into two subgroups in a random way. One subgroup gets the treatment and the other one not, but otherwise they are exactly the same. When the treatment ends and there are differences between the two subgroups, these differences can logically only be caused by the treatment.

> *This kind of study is the strongest design available in science to show causally if a treatment works. One does not need to understand what depression is, where it comes from, or what the causes are.*

Limits of this method

This sounds simple and straightforward, but such randomized controlled trials also have all kinds of problems and it is often still not completely certain if the treatment works when a trial has shown that. But it is the best design available in science to show if something works.

If treatments are not examined in randomized trials, the uncertainty if the treatment actually works is much larger. Many problems change over time, because conditions change, things happen in the personal life of a patient, the patient learns new coping skills or a talk with a friend gives new insights about the problems. That means that if you simply examine how many people who receive a treatment get better, you never know how many would have gotten better without the treatment. Therefore randomized controlled trials are very much needed to examine the effects of treatments and there are no good alternatives for such trials.

Fortunately, there are many randomized trials examining the effects of psychotherapies, and that has resulted in a lot of knowledge about these treatments.

> *Even though we still do not know what a depression is...*

6

Does “time heal all wounds”?

“It is said that ‘time heals all wounds’. But can time also heal depression? And if time can heal, is it as effective as psychotherapy? Can it be better, in some cases, not to seek treatment for mental health problems?”

A question that is harder to answer than it seems

A colleague submitted this question and asked if we could write about it. It is a difficult one that cannot be answered directly. One major complication is that we do not really know what happens when someone has a mental health problem and is willing to get treatment but does not receive it. As a result, it is largely unknown how many people with mental health problems get better without treatment, and how long that takes.

Why the answer is so hard to study

For most mental health problems, several evidence-based treatments are available, and treatment guidelines in primary care, specialized mental health care, and general medical care recommend them. This means that when a patient goes to a clinician, they will be offered treatment. That is good for patients—but it also means we can no longer examine what happens when these patients are not treated, and how many get better on their own.

There are also many people with mental health problems who do not seek treatment. In fact, most people with mental health problems never seek or receive an evidence-based treatment. In principle, we can examine what happens to them. But research shows that mental health problems tend to be substantially worse in people who do seek help than in those who do not, and there may be other differences too—for example, the social network may be stronger in those who do not seek help. This means that the outcomes of people who do not seek help cannot tell us much about how many people recover without treatment.

What the evidence does suggest

It is known that many people with mental health problems do get better without treatment. In one study (van Beljouw et al., 2010), people with depression and anxiety who perceived a need for care but did not get treatment had outcomes after

one year that were comparable to those who did get treatment. But because the two groups still differed in important ways, this cannot be taken to mean that treatment has little added value.

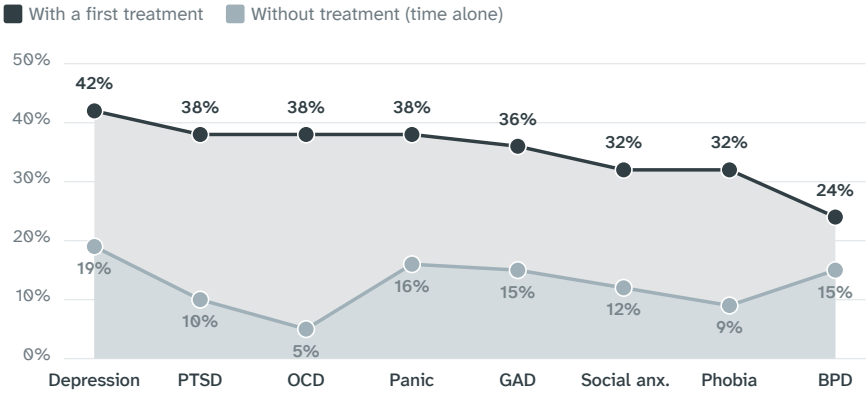
So there are no good data on how well time alone can heal these wounds. However, outcome studies in psychotherapy can tell us a little. Because good outcome studies compare therapies with control conditions in which patients are not treated, we can estimate how many people improve without treatment.

The proportion of people who recover without treatment ranges from about 9 to 19% for common disorders such as depression, anxiety, and PTSD, and is somewhat lower for OCD (about 5%). Recovery with a first evidence-based treatment is considerably higher: about 42% for depression, between 32 and 38% for anxiety disorders, PTSD, and OCD, and about 25% for borderline personality disorder. “Getting better” here means that symptoms are reduced by at least 50% from the start to the end of the study.

These proportions should be read with caution, because they come from different types of control groups (waitlist, usual care, psychoeducation, and so on). And the “with treatment” figures reflect only the first treatment. If the first treatment does

How many people improve substantially with and without treatment?

Response rates, i.e. the proportion of patients whose symptoms drop by at least half, with a first evidence-based treatment and without treatment (time alone). The gap between the lines is how much treatment adds.



Source: Cuijpers et al. (2024). Absolute and relative outcomes of psychotherapies for eight mental disorders. World Psychiatry, 23, 267–275 (Table 2, main analysis). Control conditions were waitlist, care-as-usual, or pill placebo. PTSD: posttraumatic stress disorder; OCD: obsessive-compulsive disorder; GAD: generalized anxiety disorder; BPD: borderline personality disorder.

not work, clinicians usually offer to extend it, add medication, try another approach, or change therapist. Most people stay in treatment until they are better—which can happen quickly, with a single treatment, or take several.

Weighing the decision

It is also worth keeping in mind that treatment comes with costs. It requires time, effort, and a willingness to change, and—depending on the health care system—sometimes money. It can go quickly when the first treatment works, but it can also take a long time, it can have negative effects, and in some cases it may not work at all. And some people do get better without it.

Whether or not to seek treatment is a difficult decision that requires balancing the expected benefits against these costs.

> *The most important rule is this: when a mental health problem interferes substantially with your daily life, it is worth seeking treatment.*

For example, when you can no longer work or go to school—or can only do so with great effort—or when it becomes very difficult to maintain your social or family life. You should also seek treatment if you have any thoughts of hurting yourself. When the problems interfere with your life, it is almost always worth the effort to get help.

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7

Why can't we predict who benefits from which treatment?

"As a clinician I try to follow outcome research in psychotherapy, and it seems like the whole biomedical field is moving away from randomized trials to research on who benefits from treatment. This whole move towards personalization does not seem to be happening in mental health research. Why is that?"

An old question we still cannot answer

It is not new to stress the importance of examining for whom and how therapies work, in addition to examining if treatments work. In a seminal paper from 1967, Gordon Paul already said that outcome research should focus on the question:

> *"What treatment, by whom, is most effective for this individual with that specific problem, and under which set of circumstances?"*

Since then, many scientists and clinicians have repeated the importance of examining who benefits from which treatment. But unfortunately, little progress has been made since this question was posed about 60 years ago.

There are several thousand randomized trials showing that many types of psychotherapy are effective for many different mental health problems. But we have made hardly any progress on answering who benefits from which treatment.

For example, in depression we have many different effective therapies, but it is not known which therapy is best for which patient. If you must choose a therapy for a specific patient, there is still no evidence-based recommendation that you can use. The whole biomedical field is moving towards "personalized treatments", but little progress has been made in the field of depression and other mental disorders.

The search for subtypes of mental disorders

Most research has been done in the field of depression, because depression is such a heterogeneous condition. There have been many attempts to find different 'types' of depression that would respond better to specific types of therapy, including for

example melancholic depression, atypical depression, anxious depression, early onset depression, early trauma depression, etc.

Unfortunately, none of these subtypes has been found to respond better to one type of treatment compared to another. Exceptions are bipolar and psychotic depression that do need specific treatments, and, for example for seasonal depression, specific treatments have been developed. But other than that, the attempts to differentiate different types of depression have not been successful. Treatments work on average, but knowledge on who benefits from which treatment is almost completely absent.

Three approaches to the problem

One major problem of examining who benefits from which treatment is that large studies with many participants are needed. Most effect studies are designed to show that a treatment works, not for whom, resulting in far too few participants to examine that.

One innovative approach to find more knowledge on this question is through individual patient data meta-analyses. In these studies, the data of multiple primary studies examining the same intervention are combined into a very large new dataset, which solves the problem of small numbers of participants.

A growing number of such meta-analyses are being conducted, especially in the field of depression, but only a few have found characteristics that predict who will benefit more from one therapy compared to another. None of the findings are ready to be used in clinical practice.

Another major new method to identify who benefits more from one treatment compared to the other is the use of machine learning methods in large samples of patient data in routine care. A growing number of such studies has been conducted in recent years, but again no results have been found yet that are ready to be used in clinical practice. This relates to the problem that the machine learning methods are usually too unreliable, impractical, or both, to inform practice.

A third method that can be used to predict outcome in patients is the use of very large randomized controlled trials with enough participants, and the inclusion of many characteristics that may predict outcome. A growing number of such studies is now being done, but unfortunately no characteristics have been found until now that are ready to be used in clinical care.

In summary

In summary, yes, it is not just important to examine if a therapy works, but also for whom. There has also been much research examining this question, but unfortu-

nately this research has not yet come up with characteristics that can predict which treatment is better for which patient.

Clinicians often have certain ideas about who benefits more from which treatment, but unfortunately such ideas are rarely based on good scientific knowledge. And this means that it is basically a matter of trial and error which treatment will work for which patient.

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8

Can I use AI as therapy for mental health problems?

"I have been thinking of going into therapy for a while, but I also have a lot of doubts about that. Can I try AI chatbots, such as ChatGPT, Gemini or Claude as a therapist, just to try if that works? Or is it better to go to a therapist after all?"

The short answer

At this moment, AI agents are certainly not an effective replacement for care from a mental health professional. Professionals have a license to provide qualified and safe care. AI agents can provide inaccurate and in some cases dangerous advice and cannot provide diagnoses for mental health conditions. This means that the short answer to this question from a patient is: no, AI is not a good alternative for going to a professional clinician for help with mental health problems.

> *Especially in a crisis situation, it is important not to rely on AI, but to seek immediate human help.*

What the evidence shows so far

Although there is an increasing number of studies examining the effects of using AI as a therapist for mental health problems, it is not yet known whether these interventions are effective. The first well-designed studies do show that AI, under experimental conditions (so with modifications specifically for the study) can have effects on mental health problems. That is not surprising, because there is already a long tradition of digital interventions for mental health problems. These digital interventions are based on self-help, meaning that users learn how to apply a psychological treatment to themselves. There are two broad types of such digital treatments: self-guided treatments, without any human support, and guided self-help, meaning that a human coach or clinician helps the patient work through the treatment. Both are effective when compared to control groups, but guided self-help is substantially more effective than self-guided treatments, and is as effective as face-to-face therapies in several mental health conditions. Currently it is not

known whether AI therapies (without involvement of clinicians) are as effective as self-guided treatments, or if they can be as effective as guided self-help and face-to-face therapies.

AI and the accessibility of care

If some AI therapies would indeed turn out to be as effective as face-to-face therapies, that would mean that many more patients worldwide could be provided with effective treatments. That is important, because many patients currently do not have access to face-to-face therapies. It is, however, also very much possible that AI therapies are not more effective than self-guided treatments. This would still mean that more people will get access to evidence-based treatments, but in that case AI therapies may not add very much to what is already existing. However, they may make treatments more accessible or attractive for some people.

All treatments have limits

It must be kept in mind, however, that all treatments have limited effects (on average, a 50% symptom reduction is realized in 30 to 42% of patients with a common mental disorder). Even if AI therapies can approach these numbers, there will still be many patients who will not be helped sufficiently with these treatments, and they will need additional treatment.

Using AI safely

The American Psychological Association has released an excellent guide for patients on AI agents and how to use them safely. If you are considering to use AI, you should certainly read this guide. It summarizes what you should know when you use AI, for example that such chatbots always tends to agree with you, that they are designed to keep you engaged, sound confident even when they are wrong, and that they can feel like it “knowing” you, while in reality they do not. It is also important to keep in mind most chatbots are provided by for-profit companies that stores your personal information. If you use such conversational agents, for example for organizing your thoughts and reflections, it is important to realize that mental health information from AI can be wrong, and that it cannot give diagnoses. And if you go to a clinician, be open about your use of AI.

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9

Is human contact the most important part of therapy?

"A psychiatrist in my country is very critical about mental health care and says that human contact is the most important change factor in treatments. He says that the personal story of patients does not get enough attention in treatments."

Do personal stories get enough attention?

The psychiatrist who says this seems to refer to biological psychiatry, where treatments mostly consist of medication. When psychiatrists consider mental health problems as a biological disease that can be 'solved' with medication, they indeed run the risk of simplifying the personal stories and mental health problems of patients.

However, mental health care is much broader than just the medical approaches of psychiatrists. Especially psychologists and psychotherapists are trained to listen to the personal stories of patients.

Most patients who go to mental health care have an intake of multiple sessions, in which all details of the problems, the history of the patient and their environment are described elaborately. Stating that the personal story of patients does not get enough attention is simply not true in specialized mental health organizations. It may be true for the small group of very biologically oriented psychiatrists, but certainly not for most mental health professionals.

Is human contact the most important change factor?

But when psychotherapists treat patients, is it true that human contact is the most important change factor? The answer is a clear 'no'. This assumption can only be made by someone who does not understand the basics of psychotherapy and the power of psychotherapy to help patients change.

The Dodo bird verdict

There is of course the so-called 'Dodo bird verdict', the hypothesis that all therapies have comparable effects, and that it is the 'common factors' instead of the specific

techniques that help people solve mental health problems. I wrote a separate blog about the question of whether all psychotherapies are equally effective.

First, it is not clear if the 'Dodo bird verdict' is correct. For example, there is pretty strong evidence that psychotherapies for PTSD that focus on the trauma are more effective than non-trauma-focused therapies. Also in several other disorders, it is not yet clear if all therapies have comparable effects.

The alliance is a skill, not just contact

But what is more important: the Dodo bird verdict does not say that anything works, or that it is the human contact about the personal story that makes a difference. Most researchers examining the Dodo bird verdict say that the alliance between therapist and patient is important.

One could say that 'human contact' is an essential element of the alliance. But the alliance is much more. It is a therapeutic skill in which therapists are trained, and that they can also develop with patients in difficult circumstances (think for example how complicated the alliance can be in people with borderline personality disorder).

The alliance is also not the only common factor that matters. Other common factors are, for example, the expertise of the therapist. Patients go to an expert in dealing with mental health problems and place their trust in them, which in itself is a helping factor.

The most prominent supporter of the common factors, Professor Bruce Wampold, also says, for example, that specific techniques are important as a common factor. He assumes that it is not the specific factors themselves that make the difference, but that the fact that a therapist uses specific techniques (regardless of the content) can give patients hope, clear guidelines on what to do, and a way to understand their problems.

So, is the Dodo bird verdict all about 'human contact'? Clearly not. If the Dodo bird verdict is true (which is uncertain), then it is a strong simplification of what therapy is to say that it is all about human contact.

Carl Rogers and client-centered therapy

Saying that therapy is mostly about human contact goes back to the work of Carl Rogers (1902–1987). He developed client-centered therapy, a humanistic approach in which a therapist provides empathy, unconditional positive regard, and genuineness to help clients understand themselves, grow, and reach their potential. This comes close to the assumption that therapy is all about human contact.

But client-centered therapy is not ‘just good human contact’. It is a specialization of therapy, based on a strong theoretical foundation, that requires many years of training and practice in understanding the stories of patients to help them with mental health problems.

There is quite a lot of research on client-centered therapy, which is often called counseling. Most research says that counseling is as effective as other therapies, but only when it is conducted well. If therapists only try to listen well and be empathic, it is clearly not enough, and research shows that the effects are smaller in these cases.

In summary

Is human contact the most important change factor in treatments? The answer is a clear ‘no’. It is an underestimation of the strength of psychotherapies. Human contact is an important basic requirement for therapy, but therapy has much more to offer, and can help many people with mental health problems that cannot be helped with ‘regular’ human contact or biological approaches to mental health problems.

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10

What are the real causes of change in psychotherapy?

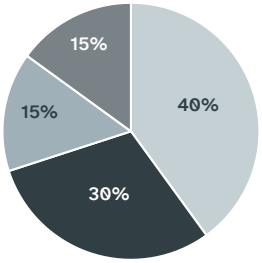
"When I was trained as a psychotherapist, I learned that change in psychotherapy is caused for 15% by specific therapeutic techniques, 30% by common factors, 15% by expectancy effects, and 40% by extra-therapeutic factors. Is that true? A colleague of mine said that this is not based on empirical data."

Where these numbers come from

These numbers come from an influential article by Lambert that was published more than 30 years ago, in 1992. Since then, these numbers are often given as a pie chart in many handbooks and training materials for clinicians. And, unfortunately, they are still used today in many training materials. These numbers and the pie chart appeal to many clinicians due to their simplicity (echoing the sentiment that "it's all about the relationship").

Lambert's model of the causes of change

The proportions often shown in training materials for the "causes of change" in psychotherapy.



Extratherapeutic factors	40%
Common factors	30%
Expectancy (placebo) effects	15%
Specific techniques	15%

Source: Lambert (1992). Note: these proportions are rough estimates and were never based on empirical data.

Why the pie chart does not hold up

However, these numbers are not based on any empirical data, and are in fact no more than rough estimates of correlates based on impressions from the literature. There is no empirical evidence to support the percentages given in the chart.

There is also a more basic problem with the interpretation of these numbers. The problem is that the four components are not mutually exclusive. For example, the therapeutic relationship can influence expectancy; a specific therapeutic technique can strengthen the alliance; patient characteristics can influence both the alliance and the response to specific techniques.

What the data can (and cannot) tell us

There are some numbers from empirical studies that could be used to make some rough estimates about what causes change, but only when one is prepared to allow for the many uncertainties and flaws of making such estimates.

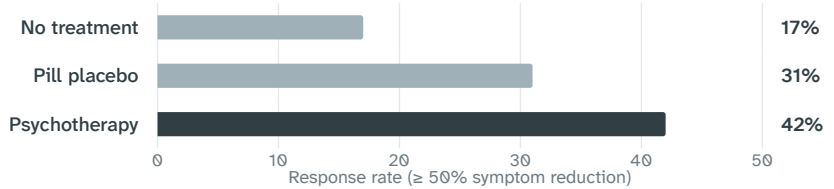
In one older meta-analysis, we examined the effects of supportive counseling for depression compared to other therapies and to control conditions (Cuijpers et al., 2012). Although this is all very hypothetical, uncertain and imprecise, one could assume that what happens in the control conditions from baseline to post-test is the 'extra-therapeutic factors' from Lambert, because that is the improvement that happens anyway, outside therapy. Based on our meta-analysis, we would estimate that 40% is caused by extra-therapeutic factors. The additional change in supportive therapy can be considered as caused by the therapeutic relationship and patient expectations; in our meta-analysis that was 50%. The specific techniques[1] were responsible for 17%.

However, nowadays we have more specific data on improvement during therapy. The most important difference between both Lambert's estimates and our meta-analysis is that we now know that there is no improvement at all in many patients. As much as 58% of patients who get therapy do not respond—only 42% do[2]. Of patients receiving no treatment about 17% respond, and those who receive pill placebo 31%. This means that specific and non-specific factors together can explain 11% of response (42 minus 31%). Based on these data, it is not possible to estimate the separate contribution of specific and non-specific factors. But, as indicated earlier, these numbers should not be used in this way, and can indicate sources of improvement only very roughly and with (too) many uncertainties.

[1]The additional effects of specific therapies above those of supportive counseling.
[2]Response defined as a 50% symptom reduction from the start to the end of therapy.

How many people respond, and to what?

Response rates (the proportion of patients whose symptoms drop by at least half) with psychotherapy, pill placebo, and no treatment.



Source: Cuijpers et al. (2021), Acta Psychiatrica Scandinavica, 144, 288–299.

The group the pie chart forgets

It should also be kept in mind that there is a small, but important, minority of patients who deteriorate during therapy. That has no place at all in the overview of Lambert, but clinically this is an important group. About 5% of patients deteriorate further during therapy. This percentage is higher when patients are not treated (12 to 13%), but it is still something that needs to be kept in mind when discussing improvement.

In summary

The most important conclusion is that the original overview of sources of improvement from Lambert is not based on empirical data and should not be used at all—also because the sources of improvement are not mutually exclusive.

More important, however, is that it suggests that change happens in all patients in therapy. But that is not the case. Many patients do not respond, and there is even a small group of patients who get worse during therapy. It is more important to be aware of this than to think about hypothetical and unclear sources of potential improvement.

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11

Will digital tools replace human contact in therapy?

"I see all these new developments in psychological treatments—digital tools, chatbots, single-session interventions, brief treatments. As a clinician I see every day how important human contact is to help patients get better. I am afraid that these developments towards digital, shorter, more efficient treatments are only useful for health insurance companies, and that patients do not get the right help anymore."

Why we cannot give everyone full individual therapy

It would indeed be wonderful if it were possible to give full individual therapy to everyone with a serious mental health problem. Unfortunately, that is not possible. There are simply too many people with mental health problems.

Currently, fewer than 40% of individuals with depression, anxiety, or substance use disorders receive any form of treatment in high-income countries, and among those who do, less than half receive care that meets minimal quality standards. Furthermore, more than 80% of the almost one billion people with mental health conditions live in low- and middle-income countries, where evidence-based treatments are only sporadically available.

It would be impossible to provide individual treatments by highly trained clinicians to all these people who currently do not get treatment. The costs would be enormous. But it would also require enormous numbers of trained clinicians, which are currently clearly not available. That is certainly the case in low-resourced settings, where often only a handful of clinicians are available for populations of hundreds of thousands or even millions.

More tools mean more people helped

Digital tools, chatbots, single-session interventions, treatments by lay health counselors, brief and ultra-brief treatments—they are all needed to help more people than are currently treated. They will not replace individual therapies delivered by highly trained clinicians. Because they are more easily available and the threshold

to use them is often lower, they will only make it possible that more people will be treated and that more people can benefit from evidence-based interventions.

The ethical question

There is also an ethical element in this issue. Suppose you give every patient with a mental health problem, such as depression or anxiety, a full course of therapy, consisting of 25 or 30 sessions (which is the case in some countries). These patients get the best treatment available, and they have an optimal chance of getting better.

However, there is no evidence that a therapy of 25 sessions is more effective than a brief treatment of 6 or 8 sessions. And digital tools with human support are also as effective as longer therapies. But if we give every patient a full 25-session therapy, that means that we can treat far fewer patients with the same amount of money and resources.

One could argue that this is unethical, especially when there are waiting lists for other patients to get treatment. But even when there are no waiting lists, shorter and simpler treatments would make resources available to treat other patient groups, in different settings, in other communities.

Therapy is effective, but not that effective

It is important to remember that psychotherapies are effective, but not that effective. More than half of the people who get treatment don't respond—and that is true for longer therapies, but also for brief, digital, guided self-help or other treatments. And there is no evidence that the response rates differ across these treatments.

That means that a lot of patients have not recovered after treatment, and that they need another treatment, an extension, or additional medication. Individual therapy, with intensive human contact, will at some point be necessary for many patients who do not get better after one or two standardized treatments that do not involve human contact. So, therapies with human contact will remain necessary to get most people better.

Some patients actually prefer digital tools

One final comment on the issue of human contact in therapy: there is also a group of patients who prefer not to have personal contact with a therapist. As one of the pioneers of digital therapies, Professor Isaac Marks, said:

> *"A computer has no eyebrows."*

It is not clear how large this group is, but there is certainly a substantial group of patients who prefer digital tools over individual therapy.

In summary

There are so many people with mental health problems that it is impossible to treat them all with individual, extensive psychotherapies. Many people can be helped with brief, digital, single-session or other therapies with less human contact. But because many patients will not recover from their first treatment, the need for intensive individual therapies will not decrease.

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12

Why are the economic costs of mental disorders so high?

"As a clinician I sometimes go to conferences, where I often hear that the economic costs of mental disorders are very high. But the treatments are not that expensive, certainly not when compared to many general medical treatments. So how come these costs are so high?"

Why the costs are so high

The costs of mental disorders are indeed very high. The main reason why that is the case is that mental disorders are 'working-age' problems. Many general medical disorders occur more often in older age, and the chance of getting them is higher as people get older. That is the case, for example, in heart disease, cancer, diabetes and many other conditions. This is different in mental disorders: they affect people during their whole life span, and can be better considered as 'working-age' problems.

Much of the costs are, therefore, associated with production losses, meaning that people with mental health conditions cannot work because of their condition (absenteeism) or are less productive when they do go to work (presenteeism). These costs are higher than only the costs of treating the mental health condition (medical costs).

How big are the costs?

It is not possible to give an exact estimate of the costs of mental disorders, because they differ substantially per country, depending on the healthcare system (universal health care or not) and the economic system. Still, a few figures give a sense of the scale:

- A recent study in the US found that the economic costs there were higher than 330 billion dollars in 2019 (Greenberg et al., 2023).
- The WHO estimates that globally 12 billion working days are lost every year to depression and anxiety, at a cost of US$1 trillion per year in lost productivity.
- Another study estimated that the projected global economic burden of depression from 2025 to 2050 will be US$12 trillion (2024 US dollars; Cao et al., 2026).

What about the individual?

These numbers are all about the costs at the population level. For individuals with depression, these numbers can be very different. If treatment is part of the universal health care in a country, individuals often do not have to pay anything, or relatively little, for treatment of mental health problems. If there is no universal health care, or it does not include mental health treatment, the costs for an individual can be substantial.

Do treatments reduce the costs?

Can treatments reduce the costs of mental disorders? In other words: are mental health treatments cost-effective? The answer is: probably yes. One problem with cost-effectiveness studies is that many different methods are used to examine whether treatments are cost-effective. However, most reviews show that psychological treatments are indeed cost-effective.

Mental health care as an investment

If mental health problems are so expensive at the population level and treatments are effective, can mental health care be seen as an investment in the economy of a country? This is indeed probably the case.

In the United Kingdom, the Improving Access to Psychological Therapies (IAPT) program was started with exactly that goal: increasing access to treatments, while the costs would be covered by reducing absenteeism and increasing presenteeism. It is not clear whether that has indeed worked, but it is certain that the health costs of IAPT are paid in large part by these economic benefits.

Developing a mental health care system is beneficial to any country, including low- and middle-income countries. In one modeling study, we found that scaling up mental health treatment for common mental disorders also leads to large economic productivity gains (a net present value of $230 billion for scaled-up depression treatment and $169 billion for anxiety disorders, in 2016).

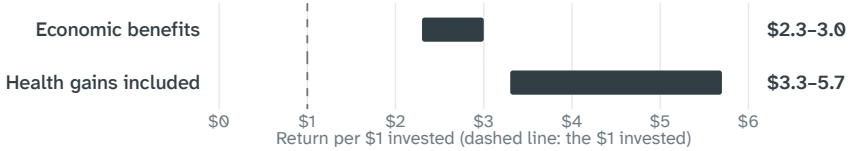
> *For every dollar invested, the return on investment was estimated to be 2.3 to 3 dollars in economic benefits. If the value of increased health was also included in the model, every invested dollar can be expected to return 3.3 to 5.7 dollars (Chisholm et al., 2016).*

In summary

Yes, the costs of mental health problems are enormous at the level of populations (apart from the personal suffering of patients and their close ones). This is not only because of the costs of treatments, but also because of production losses. Building up systems of mental health care can be seen as an investment in the economy of

What does every $1 invested in treatment return?

Return on investment from scaling up treatment for depression and anxiety worldwide. Each dollar invested is estimated to come back several times.



Source: Chisholm et al. (2016), The Lancet Psychiatry, 3, 415–424. Global return-on-investment analysis for scaled-up treatment of depression and anxiety.

a country, and can substantially improve the quality of life of those who suffer from these conditions.

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13

Do psychotherapies also work in non-Western countries?

"I am a clinician and I recently met a colleague from China, who told me she usually works with cognitive behavioral therapies when treating patients. Are these therapies not very much based on Western views? Can they also be successfully applied in completely different cultures?"

Where the research has been done

It is indeed true that most psychotherapies have been developed in North America and Europe, and are used most in Western countries. Also, the large majority of randomized controlled trials examining the effects of these therapies have been conducted in North America, Europe and Australia. However, a growing number of studies are also examining the effects of therapies in other areas of the world, especially East and South Asia, but also in Africa and Latin America.

What the studies find

Usually, it is found that the effects of psychotherapies for common mental disorders in non-Western countries are either larger than in Western countries, or comparable.

The concept of "Western" countries is not very clear, and usually this includes countries in North America, Europe and Australia. But the effects of therapies have also been examined using different categorizations of countries, including the income level of the country (high–middle–low; according to the World Bank) and the WHO regions. But the results are always the same: the effects are larger than, or comparable to, those in Western and high-income countries.

Why might effects look larger outside the West?

Some meta-analyses find that the effects of therapies are better in non-Western countries. It is not clear if that is really the case. It is possible that these therapies simply work better in (some) non-Western countries, but it is not clear why that would be so.

Another explanation could be that many studies in non-Western countries compare therapies with care-as-usual control groups. Care-as-usual in many countries

simply means that people get no treatment at all, while in many Western countries care-as-usual means that patients have access to several treatments, such as regular care provided by general practitioners or specialized mental health services.

Another explanation could be that the quality of the studies conducted in non-Western countries is often not optimal.

> *But whatever the explanation, research very clearly says that psychotherapies work at least just as well in other countries and cultures as they do in high-income Western countries. Maybe even a little better.*

Do therapies need cultural adaptation?

Are these therapies adapted to the context in which they are applied? Some studies find that cultural adaptation is needed and results in better effects. But most meta-analyses find no significant differences between therapies that have been culturally adapted and those that were not.

This should be considered with caution, however, because many studies are not very clear about if and how they adapted the treatments. It seems plausible that treatments are at least to some extent adapted in such a way that patients better understand what the basic ideas of the therapies are.

Are there non-Western therapies?

Are there no non-Western therapies at all? Yes, there are some, but not that many. The most important exception is mindfulness, which is based on Eastern philosophies and practices. But there are other notable exceptions, such as Morita therapy from Japan and the Chinese Chan-based mind-body interventions.

There are also several treatments that are based on therapies developed in Western countries but adapted for use in low- and middle-income countries. They are often made simpler and shorter, so that they can be used by providers who have not been trained as clinicians. For example, the WHO has developed interventions like Problem Management Plus, Step-by-Step, Self-Help Plus, and Doing What Matters in Times of Stress. These interventions can be delivered by trained lay-health counselors, like nurses in primary care centers.

In conclusion

Therapies that have been developed in high-income Western countries are as effective in other cultures and in low- and middle-income countries. There is no good reason to assume that therapies would not work in other contexts. It is not clear whether much adaptation is needed for treatments to be effective, although

any intervention should be adapted in such a way that patients understand the basics and consider them acceptable.

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How much of psychotherapy's effect is due to placebo effects?

"I have read that the effects of pill placebos are substantial in the treatment of depression. So can we be certain that the effects of psychotherapy are more than simply placebo effects?"

Psychotherapy compared with pill placebo

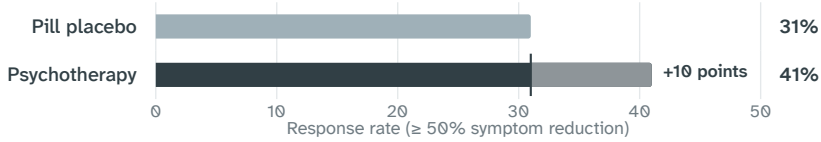
This question can be answered in a straightforward way by looking at studies in which psychotherapy for depression is compared with pill placebo. This shows that the effects of psychotherapy are larger than those of placebo, meaning that at least not all effects of psychotherapy can be explained by placebo.

In one large meta-analysis, we examined response rates, defined as a 50% symptom reduction between the start and end of therapy, in psychotherapy outcome studies, including studies in which psychotherapy was compared with placebo control conditions. We found that the response rate in people receiving psychotherapy was 41%, and in those receiving placebo 31%.

One could conclude that these findings suggest that about three quarters of the effects of therapy can be explained by placebo effects, and that the unique contribution of psychotherapy is only 10% (41% minus 31%). However, the reality is more complicated.

Psychotherapy compared with pill placebo

Response rates (the proportion of patients whose symptoms drop by at least half) in depression trials.



Source: Cuijpers et al. (2021), Acta Psychiatrica Scandinavica, 144, 288–299.

What is the placebo effect?

The placebo effect can be seen as an improvement in symptoms caused by a person's expectations of a treatment, rather than by the treatment's specific ingredients. In drug trials, the placebo usually consists of a sugar pill that looks exactly like a pill that contains, for example, an antidepressant. Patients are randomly assigned to get the placebo or the actual drug, and in good trials nobody is aware of who got the placebo and who got the antidepressant.

The placebo response rate in drug trials is comparable to the response rate in psychotherapy trials in which patients received a pill placebo instead of psychotherapy.

Expectations matter in both

The problem is that expectancies play a big role in the placebo effect, but also in psychotherapies. Many researchers assume that giving hope to patients that the treatment will make them better, and increasing the expectation that things will get better soon, is an essential part of any therapy. The conclusion that psychotherapy contributes "only" 10% to the response rates is therefore not correct.

> *The effects of placebo and psychotherapy are both caused in part by increased expectancies that patients will improve.*

Unfortunately, it is not exactly known how psychotherapies and placebos work, and the conclusion that both work at least in part through the same mechanisms is based on indirect evidence. But it should also be kept in mind that in real life, patients never get a pill placebo, because that is not a regular part of depression treatment. They do get psychotherapy, however, making psychotherapy the best way to provide such expectancies and hope to patients.

Why psychotherapy trials cannot be "double-blind"

In studies in which pill placebos are directly compared with antidepressants, all participants, clinicians and evaluators are usually masked, so that none of them knows whether they received the drug or the placebo. That is a very strong scientific design: differences between those who got the drug and those who got placebo can only be caused by the drug, because that is the only difference between the two groups.

For psychotherapies, such "double-blind" trials are unfortunately not possible, because patients and clinicians are fully aware of whether they are in the treatment or the control group. This is a key problem for psychotherapy research, for which no good solution exists.

In conclusion

Psychotherapy for depression is more effective than pill placebo, but it remains unclear how much of its effects can be attributed to specific therapeutic techniques, and how much to expectations of improvement and hope. These factors are important in both psychotherapy and placebo effects and cannot easily be separated. Because patients and therapists cannot be blinded in psychotherapy trials, it is difficult to determine the exact contribution of each.

What matters, however, is that psychotherapy can provide patients with both effective therapeutic techniques and hope for improvement.

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15

Are the benefits of psychotherapy exaggerated?

"I often hear that the benefits of psychotherapy are exaggerated because research studies tend to overestimate its effects and many patients do not improve. How effective is psychotherapy really, and is it still the best treatment option for people with mental disorders?"

Yes, the effects have been overestimated

It depends on how you look at this question. It is certainly true that the effects of therapy have been overestimated. That has several causes.

One important cause is that many studies examining the effects of therapy have 'weak spots', which in the research field is called 'risk of bias'. Effect studies should follow strict rules about how the study is conducted. If these rules are not followed correctly, this may result in an overestimation of the effects. For example, it is important that participants in a study are randomly assigned to the treatment or control group. If that randomization is not done well, this may be associated with an overestimation of the effects. Another example is that, for methodological reasons, such studies require that all participants who were randomly assigned to one of the groups are also included in the final analyses. This can also be done incorrectly. It has been shown in many studies that if a study has not solved these 'weak spots' or risk of bias, the effects are substantially overestimated.

Another problem is that studies with negative outcomes for a therapy are often not published. This may be related to researchers who prefer not to publish the data, or to journals that are not happy with negative findings. This is often called 'publication bias'. Publication bias inflates the effects of treatments, because it means that meta-analyses, in which the effects of therapies are statistically integrated, include only the positive studies.

A third problem is that many studies compare a treatment with a waitlist. If the people who receive treatment are better off than the people waiting for treatment, this can be seen as evidence that the treatment works. However, there is much research showing that waitlist control groups overestimate the effects of therapy

and result in much stronger effects compared to other control groups (such as usual care). People on a waitlist probably do not take the same actions to solve their problems as they would when assigned to usual care.

> *Together these problems have a big impact on the estimated effects of therapy. In one study we found that when we take all three problems into account, the effects of psychotherapy for depression were only 50% of those found when these problems were not taken into account.*

Many people do not benefit

It is also true that many people do not benefit from treatments of mental disorders. For depression, only 42% of those who receive treatment respond (defined as a 50% symptom reduction between the start and end of therapy). For anxiety disorders, PTSD and OCD, these numbers are between 32% and 38%, and even lower for borderline personality disorder.

But therapy is still the best option

On the other hand, psychotherapies are the best treatments of mental disorders, and they have a long-lasting impact on those who receive them. In depression, it has been found that one course of therapy has better effects at one-year follow-up than taking antidepressants for a whole year. We also found that therapy still has significant effects when compared to control conditions 8 years after the start of the therapy.

Getting therapy is also much better than getting nothing. Response rates for control conditions in psychotherapy research are between 5% and 19%, and always much lower than the response rates for therapy. Furthermore, the response rates for therapies seem low, but these come from research studies, while in practice patients get another treatment when the first one does not work, or a third one. Clinicians usually stay with patients until they are better.

In conclusion

So, are the benefits of psychotherapy exaggerated? That depends on how you look at this question. Better research certainly finds smaller effects of therapies than other research. But therapy is also the best option you have. Your therapy is usually extended when it does not work, and your therapist will do whatever they can to help you.

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CHAPTER 2

What to expect

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16

Can psychotherapy have negative effects?

"I am now in therapy for my depression for two months, but I have the idea that things are only getting worse. Is it possible that therapy has negative effects?"

A blind spot in the field

It has been thought for a long time that therapy cannot cause harm, because it is "just talking". That is also the reason that for a long time studies examining the effects of therapies have not reported adverse and negative effects. That is slowly changing now. Many researchers and clinicians now believe that negative effects do occur and that it is important to examine them better. But there are still quite a lot of gaps in the knowledge about negative effects and hardly any research on methods to prevent or reduce negative effects.

What counts as a "negative effect"?

One major problem is that there is no clear definition of what a 'negative' effect exactly is. It is clear that significant deterioration of symptoms can be a negative effect. Serious adverse events, such as suicide attempts, are also potential negative effects. But there are many other outcomes that can be considered to be a negative effect. Other negative effects that are sometimes reported by clients are for example:

- Treatment dissatisfaction
- Lack of a good working relation with the therapist
- Anxiety or rumination about therapy
- Emergence of new symptoms that were previously not present
- Stigmatization
- Perceived negative effects of treatment on family/friends

Because there is no consensus on what a negative effect exactly is, few studies have used consistent measures. This means that at this moment there is no clear overview of the different negative effects and how often they happen during therapy.

What the data say about deterioration

One type of negative effect that has been examined better in research is symptom deterioration during therapy. That means that the client feels that the symptoms are getting worse considerably. This happens for example in about 5% of clients who receive therapy for depression.

However, in the studies examining these negative effects, there are also control groups who do not get therapy. These control groups are necessary to examine how effective the therapy is compared to not getting therapy. In these control groups it was found that 13% of clients deteriorated in the same period.

> *This means that some clients can deteriorate during therapy, but the chance to deteriorate would have been higher if they would not have had therapy.*

So in reality, therapy has prevented deterioration in some clients, but has not been able to prevent it in other clients. In these clients, the deterioration would probably also have happened if they would not have been in therapy and it is not 'caused' by the therapy.

What to do if you feel worse

When you feel that things are getting worse during therapy, there are a few things that you need to keep in mind.

First, therapy can stir things up and maybe the fact that you are getting worse is part of the process and necessary to get better at the longer term.

It is also possible that the deterioration is not caused by the therapy, but would have happened anyway.

In any case, it is important to discuss this with your therapist. Then you can discuss the goals and focus of therapy, and whether the current approach is a good fit for you and your current situation. It is possible that the fit with your therapist is not right and that you for example don't feel understood or respected.

> *It is always important to take your experiences seriously and discuss them with your therapist.*

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Why does a treatment not work, while it is evidence-based?

"I have been working for several years now as a psychotherapist, and I find it important to work on the basis of the latest scientific evidence. But it happens quite often that I do an evidence-based treatment and the patient still does not improve. How is that possible with an evidence-based therapy? Maybe I am not such a good therapist after all?"

A widespread misunderstanding

It is a widespread misunderstanding among clinicians that evidence-based therapies should work in every patient. That is not only the case in mental health, but also in the broader biomedical field. The assumption is that when a therapy is evidence-based, it should in principle work for all, or almost all, patients.

If a patient does not improve, the clinician thinks that the therapy was not done as it should have been, that the manual was not followed properly. Or the therapist thinks that she or he did not follow the procedures well, or did not manage to make it work in the patient. It also happens a lot that when a therapy does not work, the therapist thinks the diagnosis was wrong, and that the whole diagnostic procedure should be started all over again. Maybe the wrong diagnosis was made, or an important comorbidity was missed.

> *The fact that a therapy is "evidence-based" certainly does not mean that all patients who get it recover.*

What "evidence-based" actually means

Evidence-based just means that the effects of a therapy have been shown in well-designed effect studies, the so-called randomized controlled trials. In such studies, patients who receive a specific type of therapy are compared to patients who do not receive the therapy, or who receive an alternative therapy. If these studies show that patients receiving the therapy are substantially better off than those not receiving it, then this therapy is called "evidence-based".

That certainly does not imply that every patient should get better from therapy. In fact, the number of patients who do not get better from evidence-based therapies is substantial.

How many patients actually respond?

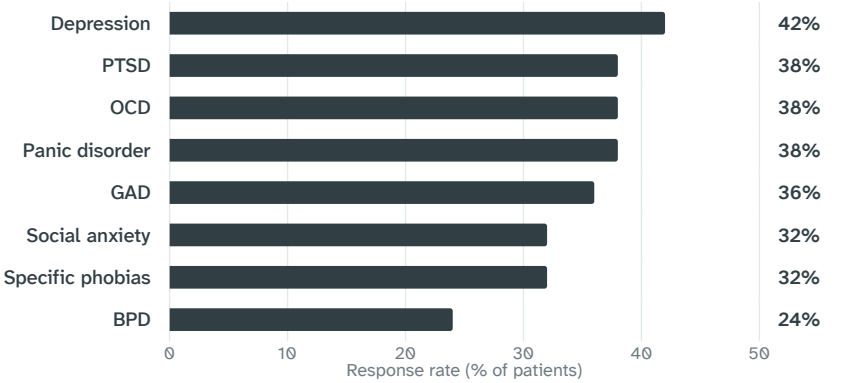
One outcome measure that is often used in research is "response". Response can be defined as a 50% reduction in symptoms from the start of therapy to the end. In a large study integrating the results of more than 400 randomized controlled trials, it was found that the response rate was 42% for people receiving an evidence-based therapy for depression. The rate for anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder was between 30 and 40%. In the control conditions, these percentages were much lower—between 5 and 19%, depending on the disorder.

These data show that evidence-based therapies certainly work, and that patients receiving therapy are much better off than those who did not get it.

> *However, there is also a large group who do not benefit, or not enough. And the therapies are still evidence-based.*

How many people respond to psychotherapy?

Response rates—the proportion of patients whose symptoms drop by at least half—for evidence-based psychotherapies across eight mental disorders.



Source: Cuijpers et al. (2024). Absolute and relative outcomes of psychotherapies for eight mental disorders. World Psychiatry, 23, 267–275.

What this means in practice

This has some important implications. First, it is important to be open with patients that therapies are helpful in many, but not all, cases. Patients can be lucky and get better during that first treatment. However, many patients will need another treatment, an extension of the current treatment, maybe they need medication in addition to therapy, or maybe they need to switch to another therapist. It is important that patients are aware of this reality, and that it is not because of them or the complexity of their case that a therapy may not work.

The other important implication is that when a patient does not respond to therapy, that is not because you are a bad therapist, did not do the therapy well, or because there is a mismatch between you and the patient. Of course that is always possible, but the fact that a patient does not respond is not evidence for it. The same is true of the diagnosis: it may be wrong, but it is more likely that the therapy simply did not work for this patient.

It is also important for you as a clinician to keep in mind that many patients will not respond to therapy, and that you need to consider next-step therapies, extension of therapies, or the addition of medication in such cases.

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18

Does therapy for depression help with other areas of life too?

"I am thinking about getting treatment for depression. I have felt depressed for a while now and it is getting harder to live my life as I did, go to work, see friends, be there for my children. But I do not only suffer from depression. If I go into therapy I also want to change other things: I find it very important to be a better dad to my children, and I feel the quality of life in general is low. Can therapy for depression also solve such problems or will it only improve depression?"

People come to therapy wanting more than symptom relief

People receiving psychotherapy for depression often find it important not only to reduce depressive symptoms, but also to improve or solve other problems in their life. Many people in therapy want to improve for example social functioning, their social relationships, their emotional functioning, increase self-awareness and self-understanding, or they want to change their attitudes towards themselves or embrace life in general more.

In more concrete terms, people also hope that the therapy will help them to be a better parent, to stop the fights with their partner or their boss, that they can learn how to be more happy, or deal better with that trauma that haunts them already for so many years. So is psychotherapy able to change such problems in addition to improving depressive symptoms?

What the research shows

Most research on psychological treatments of depression is focused on reducing symptoms of depression. There are many hundreds of well-designed outcome studies focused on that. However, many of these studies also look at other outcomes. That means that we can indeed have quite some knowledge of the effects of psychological treatment for depression on other outcomes.

There is much research that shows that psychotherapy for depression also has positive effects on:

- Quality of life in general
- Social functioning and social support
- Anxiety—it reduces anxiety symptoms
- Suicidality—it reduces suicidality
- Hopelessness and dysfunctional thinking—it improves hopelessness and reduces dysfunctional thinking

There is even a small group of studies in depressed mothers that on average find that successful treatment of depressed mothers also has an important effect on the mental health of their children and on parental functioning.

> *In these studies, it is usually found that the larger the effects are on depression, the larger also the effects on the other outcomes are. This suggests that if a treatment of depression is successful, that also other parts of life will improve.*

What about your own problems?

But these outcomes are still average outcomes for a whole group of people receiving therapy. These outcomes still do not say much about the individual problems of one person receiving therapy. There are, however, also studies that use a different type of outcome. In these studies, participants are asked to give the three most important problems they have. And then for each problem they rate how important that problem is and how much impact it has on their life on a scale from 1 to 5. These outcomes are measured before therapy and after therapy. That allows examining how much each of these individual problems has improved in terms of importance and the impact on their life. Studies using this method also show that therapies have significant effects on these very individual problems of people getting therapy.

The takeaway

> *So, the conclusion is: yes, if you get a treatment for depression that increases the chance that all kinds of other problems in your life also improve.*

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CHAPTER 3

Choosing a treatment

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Medication or psychotherapy for mental health problems?

"I have decided to get treatment for depression. I have been struggling with it for a while now, but I didn't want to get professional help and wanted to solve things myself. Yesterday I talked with a friend and she convinced me that I should get help, because that may solve my problems much faster. And it is not a sign of weakness (what I thought for a long time). But now I am doubting whether I should go for antidepressant medication or talking therapy. My friend had a lot of benefits from medication, but I think I prefer a talking therapy."

What people want vs. what people get

About three quarters of people suffering from depression and anxiety disorders prefer psychotherapy as a treatment. At the same time, the number of people taking antidepressants has been steadily increasing over the past decades. This is probably related to the fact that there are often long waiting lists for psychotherapy, the high costs of therapy, and the fact that antidepressants are often prescribed relatively easily by primary care physicians.

Which one works better?

But when you suffer from a depression, what should you do? Which of the two is more effective? The simple answer is that they have comparable effects at the short term, but at the longer term (after 1 year) psychotherapy is more effective.

> *Having one course of psychotherapy is even more effective than taking antidepressants for a whole year. At the end of that year the people who have had therapy in the beginning of that year are better off than the people who have used antidepressants during the whole year.*

But combined treatment is the real winner

This is not the whole story, however. The most effective treatment is not psychotherapy or pharmacotherapy, but the combination of the two. Combined treatment is

more effective than either psychotherapy alone or pharmacotherapy alone. And that is true at the short term and at the longer term. Adding psychotherapy to antidepressant medication probably also reduces the chance that people stop using their medication.

This does not mean that it is always better to get both treatments at the same time right at the start of a treatment. It is also very well possible to start with psychotherapy alone, and only start using drugs when the effects of therapy are not enough or the problems are not solved quickly enough.

Severity changes the calculus

But in this context it is important to distinguish between mild, moderate and severe depression. That difference is not easy to make, because all depressions are severe from the perspective of the person suffering from it. However, clinicians can differentiate depressive disorders that are relatively mild, moderate or severe. And that makes a difference for the treatment.

- In mild depressive disorders, it is generally not recommended to use antidepressants at all. Psychotherapy is the first choice treatment.
- In moderate to severe depression, combined treatment is the most effective, but starting with psychotherapy is also a good possibility.
- In some rare cases, depression is so severe that patients are not able to participate in therapy, and then treatment usually starts with medication alone.

The World Health Organization now recommends not to use antidepressants alone, without psychotherapy (unless psychotherapies are not available, like in many poorer countries).

Your preferences matter

It is always important to remember that these choices are also always related to personal preferences and choices. Some patients may prefer antidepressants above therapy, or they certainly do not want medication at all, or want to start with combined treatment right away. These are all clinical decisions that the person suffering from depression should make together with the clinician treating them.

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Is cognitive behavior therapy the best treatment for everyone?

"I finally took the step to contact a therapist, because I have been struggling with depression for a while now and I do believe that talking about my problems can help me. The therapist I talked with said that they offer 'cognitive behavior therapy' and that this is the standard therapy for depression. I have searched the internet and I saw that there are all kinds of other therapies. Is this therapy the best option for me, or is it better to try to find another therapy?"

What CBT actually is

Cognitive behavior therapy (CBT) is indeed by many considered to be the 'gold standard' in the treatment of depression. It is not one very specific type of therapy but it is better to consider it as a 'family' of therapies with many subtypes. In all subtypes, a technique called 'cognitive restructuring' is used. In this technique, clients learn to identify, challenge and change negative or distorted thought patterns. People with depression typically have a negative view on themselves, the world and the future. Cognitive restructuring helps them to change this.

Apart from cognitive restructuring, CBT can include several other techniques. One important technique that is also included in most subtypes of CBT is 'behavioral activation'. This is aimed at helping clients to identify meaningful and enjoyable activities and to stimulate them to engage in them. People with depression often have too few of such activities in their life and engaging in them has shown to be able to reduce depression. CBT often includes other components as well, including for example problem-solving techniques, social skills training and mindfulness.

Is it really the best?

Although CBT is indeed considered by many to be the best therapy for depression, there is no evidence that it is more effective than other therapies. There are several types of therapy that have been examined in more than 10 well-designed effect studies (randomized controlled trials), including:

- Behavioral activation as a stand-alone therapy (without the cognitive restructuring)
- Problem-solving therapy as a stand-alone therapy
- Interpersonal psychotherapy, which is focused on improving interpersonal relationships and social functioning
- Brief psychodynamic therapy, aimed at enhancing the patient's understanding, awareness and insight about repetitive conflicts
- Non-directive counseling, in which clients can explore thoughts and feelings in a non-judgmental and supportive environment
- Life review, specifically developed for older adults, in which they systematically go through their life course and learn how to evaluate that in a more positive way

> *There is no evidence that CBT is more effective than these other therapies.*

So why the reputation?

CBT is often considered to be the best therapy for depression, not because it is more effective than other therapies, but because it has been examined so extensively. About half of all well-designed effect studies have examined it, while other therapies have been examined much less. That means that we know very much about the effects of CBT, groups for whom it works, the format, the setting where it is delivered, the combination with pharmacotherapy and many other things. That is less so for other therapies.

Which one is right for you?

Unfortunately, it is not known who will benefit from CBT and who will benefit from another therapy. There is currently no solution for that, meaning that it will be trial and error which therapy will work for each individual. There is research on preference of clients for specific therapies, but that does not show that the preferred therapy has better effects than therapies that are offered as a standard.

This means that there is no evidence that CBT is a better treatment than other therapies, but it has been examined extensively, and it is a good choice to start a treatment with.

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21

Are all psychotherapies equally effective?

"As a clinician I try to follow new research that is published, and I often see that trials and meta-analyses comparing different therapies usually do not find any significant differences between them. Doesn't that mean that all therapies work equally well, and that human support is the most important factor in therapy, regardless of type?"

Many comparative studies find no differences—but the picture is more complex

It is true that many trials and meta-analyses examining the relative effects of different types of psychotherapy find no significant differences between treatments. However, there are several important points to keep in mind when reading these studies.

First, not all meta-analyses find that the effects of therapies are comparable across all mental health conditions—several do find significant differences. Second, if all therapies truly had comparable effects, their relative effects should also point in the same direction, and the variability between those differential effects (heterogeneity) should be small. That is certainly not what all comparative meta-analyses find.

The statistical power problem

Another important problem with these studies is that they almost never have the statistical power to identify differences between therapies—meaning that far too few patients are included. A randomized trial comparing two therapies needs more than 500 participants to be able to detect a small but clinically relevant difference. Such trials are hardly ever conducted in the psychotherapy field. Even when the results of such trials are pooled in a meta-analysis, the combined statistical power is in most cases still insufficient to identify clinically relevant differences.

> *"No significant difference" is not the same as evidence that two treatments are equivalent. In most cases, the study simply was not large enough to detect a real difference if one exists.*

What are "bona fide" treatments—and why does it matter?

One important problem is that some therapies in research are often designed to fail. They are created merely to show that the "real" therapy is more effective by comparison—these are sometimes called "intent-to-fail" or non-bona fide treatments.

Bona fide (Latin for "in good faith") treatments are therapies that are genuinely developed with therapeutic intent: theoretically grounded, structured, and delivered by trained clinicians. Non-bona fide treatments, by contrast, are minimal comparison conditions that were never expected to work well. Because non-bona fide treatments are often less effective than serious therapies, including them in trials and meta-analyses can create the appearance of differences between therapies where none may actually exist.

Proponents of the bona fide distinction argue that all differences between therapies can be explained by the inclusion of non-bona fide treatments. This is indeed a good argument—but it does not explain all the differences found in the literature, nor the remaining heterogeneity, and it does not resolve the problem of statistical power.

"Equally effective" does not mean "anything goes"

Perhaps the most important point to keep in mind is that all bona fide therapies are well-developed, standardized, and delivered by trained clinicians. Even if all therapies have comparable effects, that does not mean that a therapist can simply do whatever they please. Only well-developed and standardized therapies have been shown to work. Whether an unstructured approach would be equally effective has not been examined, and it is not known whether that works just as well.

Different roads can lead to the same destination

Even if therapies have comparable effects, that does not mean they work in the same way. It is possible that "many roads lead to Rome"—that mechanisms differ even when outcomes are the same.

For example, depression is a problem that affects many different areas of life. When someone learns to solve problems more effectively, that may lead to more positive thinking, more pleasant activities, and less depression. But increasing pleasant activities may also result in more positive thinking, better problem-solving skills, and less depression. And more positive thinking can itself lead to more pleasant

activities, better problem-solving skills, and less depression. In such cases the mechanisms are completely different, but the effects are the same.

What happens when standard therapies are not enough?

It should also be kept in mind that most research focuses on protocolized and manualized therapies—and the effects of these therapies are limited. Across most mental disorders, response rates fall between 30 and 42%: roughly that proportion of patients see their symptoms halved by the end of treatment. This means that many patients do not get better, even after two or three treatments.

In these cases, the clinical experience of the therapist becomes even more important, and simply knowing how to conduct protocolized treatments is not enough. Equally, being empathic, non-judgmental, and reflective is not sufficient either, because those elements were already part of the earlier treatment(s). The clinician will need to discuss the next options, examine the patient's personal situation more deeply, and search for new potential solutions. Clinical experience and a thorough understanding of the individual's specific mental health problem is essential in these cases.

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22

How do I find a good therapist?

"I have thought for a long time about whether I want to go into therapy, and I have now decided that the time has come. But how can I find a good therapist?"

Why research cannot answer this directly

That is a very good question, and not an easy one to answer. Unfortunately, research cannot help much in this process. It is very clear from research that so-called therapist effects exist, meaning that outcomes vary depending on the therapist. There is also research showing that some therapists are better at helping people with one type of problem, while others are better at helping people with a different type. However, there is currently no evidence-based rule that can tell an individual patient which therapist will be best for their particular problem.

Even so, there are a few principles that can help.

Check the license and the experience

First, when you look for a therapist, make sure they hold the correct license to provide therapy. Which license is required depends on the country or state where you live.

A second general recommendation is to find a therapist who has experience with the type of problem you are dealing with. A therapist specialized in eating disorders may not be the best choice if you have depression or personality problems. It can be difficult to know in advance exactly what kind of mental health problem you have, because assessing the diagnosis is usually one of the first parts of treatment. Still, most patients do have a general idea of the problem they are dealing with.

Look for evidence-based treatments

When you search for a therapist, it is also important to choose someone who uses evidence-based treatments. Many therapists indicate on their websites whether they focus on such treatments. If a therapist does not describe their methods, or if those methods are not evidence-based, it is less certain that their approach will really work for you.

> *Be cautious of promises of rapid cures, unusual claims, or too much focus on a single method as the solution for everything.*

The practical issues

Then there are the practical matters. In some universal health care systems, psychotherapy is part of the care provided to anyone, sometimes after referral by a general practitioner or another doctor. In other situations, it may be covered by a health insurance plan. However, psychotherapy is often not included in insurance plans, and then the patient has to pay for it themselves.

Another important practical issue is the waiting list. In some places, patients must wait a long time for a first appointment. Most therapy is also provided during working hours, so if you have a job, you may need to take time off or make other arrangements.

What to look for in the first meeting

When you have your first meeting with a therapist, you can check whether this is what you were hoping for. Ask, for example, whether the therapist has much experience with patients like you. You can ask what the treatment will look like, whether the therapist expects it to work in your case, and what can be done if it does not.

During this first meeting, try to get a sense of whether the therapist seems transparent and collaborative, is open to feedback, can explain the therapy and why they think it will work, and makes you feel both understood and challenged. Be careful if the therapist claims that only their method will work, or becomes defensive when questioned.

Keep evaluating your progress

Once you decide to start with a therapist, evaluate your progress regularly. A good therapist will review progress after a few sessions, but if they do not, you can always ask for it. And if you feel that you are not making enough progress, do not hesitate to discuss this with the therapist. Another treatment, an additional therapy, or even a different therapist may be a better option if things are not working for you.

23

Are long-term therapies better than brief symptom-focused therapies?

"My first therapy session is scheduled for next week. My therapist has said that cognitive behavior therapy is best for me, because of my depression. But a friend told me that this therapy is brief and only focused on symptoms. She said that long-term psychodynamic therapies are better, because they do not only focus on the symptoms but also on the deeper causes of why I am depressed. Is that true?"

What we know about brief therapies

There is a great deal of evidence that brief psychotherapies—including cognitive behavior therapy, but also interpersonal psychotherapy and behavioral activation—are effective in reducing depressive symptoms. Such therapies often consist of between 6 and 24 sessions. They also have significant effects on quality of life, social functioning, social support, self-esteem, anxiety, and several other outcomes.

These therapies typically focus on current problems and try to change how patients think or act, so that they can handle problems better. Learning about depression, and learning skills to cope with problems, is a key element of most brief therapies.

Whether these therapies also affect the "deeper causes" of mental health problems is not known—because the causes of depression itself are not known. Many risk factors have been identified, but it is still unclear how they lead to depression, and why one person becomes depressed while another in comparable circumstances does not.

What long-term therapies aim to do

Longer-term therapies, including psychodynamic and psychoanalytic therapies, have a different focus. They seek to understand how unconscious feelings, conflicts, early relationships, and habitual ways of relating influence current emotions and behavior.

There are also brief psychodynamic therapies that use these techniques to help people with depression or other mental health problems, and there is quite a lot of

evidence that they are effective. Most research suggests that brief psychodynamic therapies have effects comparable to those of other brief therapies, including cognitive behavior therapy.

The evidence gap for long-term therapies

Unfortunately, there is very little controlled research on the effects of long-term therapies for most mental health problems. This means that it is not known whether long-term therapies are effective for depression or related problems, and there is too little research to show whether they produce better outcomes than brief therapies. It is simply not known.

Long-term therapies are also very difficult to examine. To do good outcome studies, patients need to be randomized to a treatment or a control condition. Patients who want an intensive therapy, such as psychoanalysis, usually do not want to be randomized to a control group—and if they agree to it, they are probably not that motivated to undergo psychoanalysis in the first place. A further problem is that it is very difficult to follow patients for several years, during which their lives change because of the life events that happen to everyone.

> *Because long-term therapies are so hard to study, we cannot say that they work—but we also cannot say that they do not.*

The exceptions that have been studied

Some longer-term therapies have been examined in well-designed outcome studies—for example, dialectical behavior therapy and schema therapy for borderline personality disorder. These therapies easily have more than 100 sessions and last more than a year. In these studies, patients are compared with the "usual care" they would otherwise receive, and overall these therapies have small but clinically highly relevant effects. Unfortunately, such studies have hardly been done for depression or other common mental health problems.

What this means in practice

For patients with depression, it is therefore usually recommended to start with a brief therapy. Cognitive behavior therapy is a good choice, because there is a large body of research showing that it works.

However, brief therapies do not work for everyone. It is quite possible that someone is not recovered after two or three brief therapies, or after adding antidepressants to the treatment. In such situations, it can certainly be worthwhile to consider a therapist who specializes in longer-term therapies. There is no evidence that these therapies work—but by that point the briefer therapies have not worked either, and many patients are understandably willing to try anything that might help them.

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24

Is psychedelic-assisted psychotherapy effective?

"I have been severely depressed for several years, and no treatment has really worked. I am desperate and I need something to give me hope. I read online that psychedelic-assisted therapy may be able to help me. Is that true? Are these therapies effective?"

When you are desperate for something that works

When someone has been severely depressed for a long time, it is completely understandable that this person wants to do anything to get better. In such a situation, psychedelic-assisted therapy can indeed be one of the options that can be tried. There is still much that is unclear about the effects, and it certainly will not help everyone, but it is completely understandable that in situations like this, patients want to try anything that may help them.

What psychedelic-assisted therapy is

Psychedelic-assisted therapies have received growing attention in recent years as possible treatments for mental disorders. These therapies combine psychotherapy with psychedelic substances such as psilocybin, LSD, ayahuasca, or ecstasy (MDMA). The idea is that these substances may enhance the effects of psychotherapy by changing perception, mood, and cognitive processes in ways that could help patients engage more deeply with treatment.

A long and interrupted history

Research on psychedelic therapies first emerged in the 1950s and 1960s. However, this work largely stopped after psychedelics were classified as illegal drugs by the United Nations in the 1960s and 1970s. At the same time, medical research regulations became stricter after the thalidomide scandal. The studies conducted during that early period generally did not meet modern scientific standards and included very few well-designed effect studies—the so-called randomized controlled trials (RCTs).

Over the past two decades, interest in psychedelic-assisted therapies has returned. Most research has focused on the use of psychedelics for depression and MDMA-assisted psychotherapy for post-traumatic stress disorder (PTSD). A smaller number of studies have also examined their effects on other conditions, including obsessive-compulsive disorder, borderline personality disorder, body dysmorphic disorder, and alcohol use disorder.

What the evidence shows so far

The available evidence appears promising. In depression and PTSD, about 20 RCTs have compared psychedelic-assisted therapies to placebo or waitlist control conditions, and the effects of the therapies were large. These findings have led some researchers and commentators to describe psychedelic-assisted therapies as a potentially transformative development in mental health care.

> *The available evidence appears promising—but it is important to note the limitations that make it difficult to draw firm conclusions.*

It is, however, important to note that there are important limitations that make it difficult to draw firm conclusions. First, the number of studies is still small, and the total number of participants is limited. Strong evidence usually requires more large, well-conducted trials, which are still lacking in this field.

Second, several methodological concerns affect the credibility of the findings. Like many areas of mental health research, psychedelic studies may be influenced by small sample sizes, selective reporting of outcomes, conflicts of interest, and several other biases. These factors can lead to overly optimistic estimates of treatment effects.

The problem of long-term effects

A particularly important issue is the lack of long-term follow-up data. Psychedelic substances are known to have powerful short-term effects—which is not surprising, because they are also used as party drugs. However, from a clinical perspective it is much more important to know whether the benefits persist after the immediate drug effects have disappeared. So far, few studies have examined long-term outcomes, and these effects are very uncertain.

The problem of comparison groups

Another major challenge concerns the use of control groups. Because psychedelics produce obvious psychological effects, participants usually know whether they received the active treatment or a placebo. Many participants also enter studies with positive expectations about psychedelic therapies, and may be disappointed if they

are assigned to a control condition. These expectations could influence outcomes and make it difficult to determine the true effectiveness of the treatment.

It also matters that participants who end up in the control group of an RCT can be disappointed, because they had hoped to receive the psychedelics. This disappointment—or perhaps finding other ways to obtain psychedelics—changes the control group. This makes it difficult to compare psychedelic-assisted therapy to the care patients usually get.

In summary

Psychedelic-assisted therapies may have the potential to improve the treatment of mental disorders, particularly depression and PTSD. However, the current evidence base is still limited, and important methodological problems mean that we cannot yet conclude that these therapies are truly effective in helping patients in the longer term.

Because this is a fast-moving field, the evidence is best followed as it develops. At Metapsy we provide access to a continuously updated, living synthesis of the trials on these treatments maintained by the SYPRES collaboration.

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25

Can a single-session intervention already help with mental health problems?

"Is it true that single-session interventions are effective? How is that possible, when even long therapies have modest effects? As a clinician I find this hard to believe."

The evidence

There is substantial evidence that single-session interventions (SSIs) can be effective in people with mental health problems. Several hundred randomized controlled trials have shown that SSIs, on average, have small but significant effects. These studies have been conducted in children, adolescents and adults, and across several mental health problems, including depression, anxiety, externalizing problems, eating problems, and substance use problems.

How can one session work?

SSIs are probably not equivalent to a full course of psychotherapy. Their effects are typically smaller. Furthermore, the longer-term outcomes are not so clear, and it is quite possible that the effects fade relatively fast.

Their effects may be related to the fact that the association between the number of sessions and the outcome of longer therapies is not linear, and that much of the benefit of therapy occurs early in treatment. SSIs could then generate much of that change in only one session.

In fact, there is no evidence at all that the number of sessions is associated with the outcomes of therapy, at least in depression. In a recent meta-analysis, we examined whether the number of sessions, total contact time, and the length and frequency of sessions (number of sessions per week) were associated with the effects (Ciharova et al., 2024). We found that a higher frequency was associated with better outcomes, while the number of sessions, contact time and length were not.

What makes an SSI different from a short therapy

We should also keep in mind that SSIs are not a regular therapy that simply stops after one session. They typically focus on one specific mechanism—such as behavioral activation, exposure, or problem solving—that can be applied in daily life right away. They are also designed with the assumption that each encounter could be the only encounter.

Why SSIs matter: scalability

The major benefit of SSIs is that they are highly scalable, meaning that they can be applied with relatively few resources and that the threshold to use them is relatively low.

Most people with mental health problems do not have access to evidence-based treatments. More than 80% of people with mental health problems live in low- and middle-income countries, where evidence-based treatments are typically not available at all. But also in high-income countries, many people with mental health problems do not use evidence-based treatments. Less than half of those with a diagnosis of a mental disorder in high-income countries get an evidence-based treatment, and these numbers are even lower in specific high-risk groups, such as older adults, adolescents and young adults, ethnic minorities, and people from groups with lower socioeconomic status.

It is important, therefore, to develop interventions that are scalable. Even when they are somewhat less effective than full treatment, they can still have an enormous impact on mental health.

> *If these interventions are used by many people, the total impact can be higher than the impact of very effective treatments that are used by only a small, selected group of patients.*

SSIs are one of the most promising types of scalable interventions, next to digital tools and, for example, treatments delivered by trained lay counselors. They can be used in lower-income settings as full treatment (it is better to receive an SSI than to receive nothing), but also, for example, for people on waiting lists for treatment, and as an entry point to mental health care.

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26

Are therapists with a license better than those without?

"I have been trained as a psychologist, but I do not (yet) have an official license to treat patients. I have read scientific papers saying that the outcomes of therapies are also good when therapists have not been trained as clinicians. So am I currently doing just as well as a licensed clinician?"

A license is more than a university degree

In many countries there is indeed a difference between a university-level education in psychology and a professional license or registration required for independent clinical practice. Licensed psychologists have fulfilled additional professional requirements, including, for example, supervised clinical training and assessment of clinical competence. Licensed psychologists are legally authorized to practice within the scope of their license.

Can therapists without a license deliver therapy?

Are the outcomes of therapies conducted by licensed psychologists better than those of psychologists without a license? There is much evidence that therapists without a license can successfully deliver psychological treatments. There are many trials in which students who are still in training deliver therapies successfully, and there are also many studies in which trained 'lay-health counselors' deliver psychological treatments.

So there is no doubt that therapies can be delivered successfully by clinicians without a license. It is less certain whether the effects are completely comparable between licensed therapists and so-called 'paraprofessionals', because there is too little high-quality research examining this question directly. But it is certain that treatments delivered by both professional and paraprofessional therapists are effective.

Why the licensed clinician's role is broader

However, it has to be kept in mind that the treatments examined in outcome studies are highly manualized and protocolized. The professional and paraprofessional

therapists who deliver them have to follow the protocols as well as possible. That is not easy and requires skills, but it is relatively simple compared to the other work of licensed clinicians.

Licensed clinicians also have to do diagnostic work: to examine what exactly the problems of a patient are, the background, potential causes, and the clinical history. Furthermore, a licensed clinician has to decide during therapy whether everything is going well—changes, dangers, potential suicidality, and whether additional help is needed. After therapy, licensed clinicians have to make decisions about what will happen next: is everything solved now, is additional treatment needed, maybe relapse prevention? And last but not least, a licensed clinician has the legal responsibility to make sure that the treatment is done well.

Some therapists are better than others

Apart from the question of whether the effects of therapies differ for licensed therapists and those without a license, it is also important to know that the effects of therapies differ between therapists. Research has consistently shown that such 'therapist effects' exist. It has been estimated that between 5 and 8% of the outcomes of therapies depend on the therapist. That means that there are 'good' therapists and 'better' therapists, and that this can make a difference for patients.

It is less clear what exactly makes a therapist good or better, because the methods to examine this are complicated, require very large studies, and there are no designs for scientific studies that can identify such characteristics with certainty. There is, for example, little evidence that therapists get better with more experience, but it is also very complicated to be completely certain of such a finding.

Matching patients to therapists

There is some research showing that matching patients to therapists may improve the outcomes of therapies. In a well-designed study, therapists were classified as effective, neutral or ineffective across twelve problem domains, based on their historical cases. In the trial, patients were either randomized to a therapist who was effective in the problem domain of the patient (matched care), or pragmatically to any therapist. The matched care was found to be significantly more effective in terms of symptom reduction, functional impairment and global distress, with no adverse events.

In summary

So, yes, there is much evidence that therapists without a license can successfully deliver psychological treatments, and there is no evidence that therapies delivered by licensed therapists are more effective. However, the work of licensed therapists

is much broader than only providing protocolized treatments. And it has to be kept in mind that the effects of therapies also differ between individual therapists, although it is not very clear what the characteristics of the best therapists are and what differentiates them from others.

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Is psychotherapy effective in severe depression?

"I often treat patients with severe depression, and I wonder whether psychotherapy is effective enough for these patients. Should I offer psychotherapy as a treatment on its own, or is it better to combine it with antidepressant medication?"

Psychotherapy is effective, and even more in severe depression

The simple answer to this question is: yes, psychotherapy is certainly effective in the treatment of severe depression. There is even evidence that the effects of psychotherapy are larger when depression is more severe.

Psychotherapies also work in mild depression, and even in subthreshold depression, when a patient does not meet the criteria for a major depressive disorder. But they work even better in severe depression, meaning that in outcome studies the difference between people who received therapy and those in control conditions is larger.

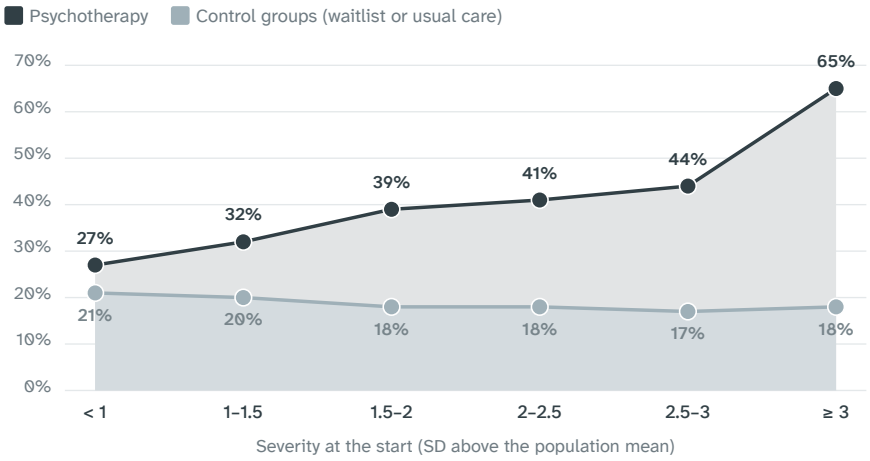
In a large meta-analysis in which we pooled the results of 387 effect studies, we found that the response rate (defined as a 50% symptom reduction between the start and end of therapy) was 27% when depression was mild. Mild depression was defined as less than one standard deviation above the mean in the general population. In severe depression (at least three standard deviations above the population mean), the response rate was 65%. In the control conditions (waitlist or usual care), the response rate varied only very little (between 17% and 21% across all levels of severity).

When psychotherapy is not (yet) possible

Psychiatrists often say that they see many patients who are so severely depressed that psychotherapy is not possible. For example, when someone is extremely depressed and also has psychotic symptoms, or when depression is so severe that someone is very apathetic, psychotherapy is indeed not feasible, and patients should first get pharmacological treatment; when this starts to work, psychotherapy can be considered.

Psychotherapy helps more when depression is more severe

The response rate, i.e. the proportion of patients whose symptoms drop by at least half, by how severe the depression was at the start.



Source: Cuijpers et al. (2026). Does baseline severity interact with the effects of psychotherapy for depression? Journal of Affective Disorders, 399, 121106 (Table 3). Severity is expressed in standard deviations (SD) above the mean of the general population.

However, whether or not psychotherapy is possible in severe depression should be assessed by experienced psychotherapists, who often see more possibilities to treat such patients, even though they seem unable to have therapy. Several psychotherapies have been found to be effective in the treatment of severe depression, including CBT, third-wave therapies, behavioral activation therapy, interpersonal psychotherapy, problem-solving therapy and psychodynamic therapy.

Combined treatment is usually best

Although psychotherapy is effective in severely depressed patients, the combination of psychotherapy and antidepressants is the preferred treatment in most cases. The effects of combined treatment are larger than those of psychotherapy and pharmacotherapy alone, both in the short and in the long term. That also means that pharmacological treatment alone is suboptimal and should be avoided, except in the rare cases where it is really not possible.

Severe depression does not need more complicated therapy

There is no evidence that severe depression predicts a poorer treatment response, although patients may remain more symptomatic after treatment. There is also

no evidence that severe depression requires more intense or more complicated psychological treatments. There is some evidence suggesting, for example, that behavioral activation, a relatively simple and straightforward treatment of depression, is at least as effective in severe depression as cognitive behavior therapy.

Severe depression is not the same as chronic depression, although the two do not exclude each other. Chronic depression is more complex and does require more intensive treatment, for example with the Cognitive Behavioral Analysis System of Psychotherapy (CBASP). CBASP was specifically developed for the treatment of chronic depression, and several studies have shown that it is indeed effective.

In conclusion

Severe depression is not a reason to withhold psychotherapy. On the contrary, research suggests that patients with more severe depression may benefit even more from psychotherapy than those with milder symptoms. Although combined treatment with psychotherapy and antidepressants is the best option, psychotherapy alone can also be effective. In patients with very severe symptoms, medication may sometimes be needed before psychotherapy can begin, but this should not be assumed without careful assessment.

> *The important message is that patients with severe depression should have access to evidence-based psychotherapy, rather than being offered medication alone simply because their depression is severe.*

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Can self-help books help with mental health problems?

"I have been struggling with depression for some time and have noticed that there are hundreds of self-help books that claim to help people overcome depression. Can reading a self-help book really help me feel better, or do I need professional treatment? And how do I know which books are actually effective?"

Very popular, but rarely tested

Self-help books are very popular. In the United States alone, almost 19 million self-help books were sold in 2019, and the number of available books increased substantially over the preceding years. One study found that the sales of self-help books tripled between 2001 and 2021 in the UK (Nehring, 2024). Many of these books aim to help people overcome mental health problems, such as depression and anxiety. Can these books really help people suffering from mental health problems?

Unfortunately, there is very little research on the effects of self-help books. In order to examine the effects of self-help books, randomized controlled trials are needed in which people with mental health problems are randomly divided into a group who get the book and another group who do not. Such studies have hardly been done, meaning that we just don't know whether most of these books work. But there are a few exceptions.

Two books that have been tested

One famous exception is the book Feeling Good by David Burns, first published in 1980, of which several million copies have been sold. Several randomized trials have examined the book, and these found significant effects, comparable to those of face-to-face therapies. Another exception is the book Control Your Depression by Peter Lewinsohn (1980), which has also been examined in a few trials, with good results.

However, the studies examining the effects of these books did not just provide the book to people with depression; they also provided brief weekly phone calls

to discuss progress, homework and questions from the readers. These phone calls probably helped to keep the patients involved and encouraged them to continue working on the materials. One study in which only self-help materials were provided to patients in primary care, without any further support, did not find any benefit of these materials (Salkovskis et al., 2006).

What digital interventions tell us

Since the rise of the internet, much research has been conducted on digital interventions, which typically provide patients with information comparable to that in self-help books. Although these digital tools are not exactly the same as self-help books, they are very similar, in the sense that information is provided to patients on how to apply a psychological treatment to themselves. These digital interventions can be either guided by humans or unguided.

It is well established that guided digital tools are as effective as face-to-face therapies, and that unguided tools are effective, but with smaller effects than guided tools. This illustrates that learning how to apply a psychological treatment to oneself may help some people to overcome mental health problems, although this has not been established very well for self-help books.

What about chatbots?

Currently, more and more patients use chatbots, such as ChatGPT, Gemini or Claude, to discuss their mental health problems. This may be helpful, but there is too little research yet to be certain. The use of such chatbots can also be dangerous, because they are programmed to confirm what you say and not to challenge you. The dangers of regular chatbots are well documented.

Not a replacement for professional help

An important issue for patients is that self-help books can never replace professional help.

> *If you suffer from a mental health problem that interferes with your daily activities, at work, at school, or in your relationship with your partner or family, you should seek professional help. No self-help book, digital tool or chatbot can replace that.*

In conclusion

Although self-help books are very popular, remarkably little is known about their effectiveness in treating mental health problems. Research on a few scientifically based self-help books, and the much larger body of research on digital interventions, suggest that people can benefit from learning how to apply psychological

treatments to themselves, especially when some human support is provided. However, self-help books should not be considered a substitute for professional help when mental health problems substantially interfere with daily life.

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CHAPTER 4

Special populations

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Are psychological treatments effective in older adults?

"My father is 78 years old and is complaining about mood problems. He is physically healthy and as far as I can see very active, but he still says his mood is low. Could he benefit from therapy, or does that only work in younger people?"

An old assumption that turned out to be wrong

It was assumed for a long time that therapies do not work in older adults, because of rigidity in thinking, entrenched personality traits or cognitive decline. Modern research has, however, shown that this simply is not true.

> *There is no evidence whatsoever that the effects of therapies are smaller in older people than in younger adults.*

There are even quite a few studies in older adults above 75 years of age which show that psychotherapy works for them. That means that those who receive psychotherapy are better off than people who receive usual care or are on waiting lists for psychotherapy. And that is true in all adult age groups, with no significant differences between adult age groups (therapies are less effective in children and adolescents, but that is another matter).

Which therapies have been shown to work?

There are several types of psychotherapy that have been shown to be effective:

- Cognitive behavioural therapy—the best known type, in which patients learn to think more positively about themselves, about their life, and about their future.
- Behavioral activation, in which they learn to do more positive activities that make them feel good.
- Problem-solving therapy, in which they learn to cope with their most important problems in a systematic way.
- Psychodynamic therapy, in which they explore unconscious thoughts, emotions, and early life experiences to gain insight into how their past influences their life and their problems.

- Life review therapy—one type of therapy that was specifically developed for older adults. In this therapy, patients systematically go through their life course and try to validate each of these phases of their life and evaluate them in a more positive way.

Unfortunately, there is very little knowledge about who benefits from which therapy. That means that it cannot be predicted if a patient will get better through one therapy or another.

Even in residential settings

Most studies in older adults with depression are done in people who live independently in the community. But there are also some studies for older adults who do not live independently anymore, but who live in nursing homes or residential homes. These studies show that psychotherapies also work in older adults who live in such homes.

What "working" actually means

That these therapies work does not mean that everyone benefits from them. Outcomes are often measured in terms of response, which means a symptom reduction of 50% between the start and the end of the therapy. It has been estimated that 42% of the people who get therapy respond. This is not a fixed percentage but only the mean. It has been found for example, that the proportion of responders is higher in people with more severe depression.

About 25% of patients are completely recovered, meaning that there is no difference with people without depression anymore. That means that a lot of people who get therapy are not better after one treatment, and these people need another therapy. Maybe they need to combine the therapy with antidepressant drugs, or they need an extension of the current therapy.

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What to do when my partner does not want to get treatment?

"Since his retirement my husband is very depressed. He hardly gets out of his bed, is grumpy all the time, and avoids any human contact. But he does not want to get help. I have tried everything, but he refuses even to see his general practitioner. What should I do?"

Avoiding treatment is more common than most people think

It is well known from research that a large part of people with depression do not want to get treatment. It has been estimated that less than 40% of people with depression, anxiety, or substance use disorders receive any form of treatment. There are several groups in which the uptake of treatments is even lower. That is for example the case in adolescents, young adults and students, older adults, minority groups, and groups with lower socioeconomic status. And that is the current situation in high-income countries. In low- and middle-income countries the uptake of treatments is much lower.

Why people don't seek help

There are many reasons why people don't seek treatment. In many countries there are simply no clinicians available, or patients do not have the resources to pay for treatment. But there are many other reasons why people with depression don't seek treatment, even if these are available and affordable. Many people do not believe that talking can solve their problems, they do not trust clinicians, they deny that they are depressed, they think that talking with friends is just as good or believe that the problems will go away after a while.

> *Reluctance to seek treatment is also a characteristic of depression. Someone with depression is pessimistic about many things, including the effects of treatments.*

What you as a partner can do

The patient must decide for themselves if they want treatment. You as a partner cannot make that decision. Treatments can only work when the patient is motivated to get it. What you can do as a partner is say what the benefits of treatment are, that most people with depression get better when treated. You can also point at the consequences that the depression has for you and others in your family.

> *But in the end, it is up to the patient to make this decision.*

How to support without making things worse

But there is more that you can do. You can learn yourself about depression, what it is, where it comes from, and what can be done about it. It is also important not to try to "treat" the patient, by giving advice about what to do and what not to do. Advice to interpret things less negatively usually doesn't work and can make the patient feel even more helpless. It is important to avoid critique and too much involvement and try to "let the patient alone" more. You can also make life simpler, avoid complicated decisions, make daily schedules, and try to stick to fixed times for meals and other joint activities.

Take care of yourself

Another important thing to do is take care of yourself. It is well known from research that many partners of patients with depression become depressed themselves after a while. It is important, therefore, to make clear to the patient what you want and do not want to do as caregiver. That gives clarity for your partner but also for yourself. And make sure that you have your own life and continue to do the things that are important for you. If needed, you can also ask professional help for yourself.

A note on the evidence

Several of the recommendations that are given are not based on evidence about what works for caregivers and what not, but they are all based on a considerable body of clinical experience. If you are Dutch, you can download a digital copy of a book that I have written for relatives of people with depression, based on clinical work with relatives of people with depression. The book has many concrete examples and case descriptions. You can find it here.

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Do psychological treatments work in adolescents?

"My son is 16 and he is clearly depressed for a while now. He doesn't want to go to school and he stays in his room all day. I want to seek treatment for him. But do these treatments work in adolescents, or do they only work in adults?"

Yes, these treatments are effective

Yes, treatments of depression in adolescents are certainly effective. Many well-designed studies have shown that psychotherapies are effective in adolescents. And based on this research, psychotherapies are recommended in all guidelines for clinicians on how to treat depression in adolescents. There are, however, several issues that are important to know about psychotherapy for depression in adolescents.

Why the effects can look smaller than in adults

The effects of treatments are usually examined by comparing such treatments with control conditions in randomized controlled trials. A treatment is considered effective when participants in the treatment group are doing better than those in the control group, who did not get the treatment. These studies have shown that psychotherapies for adolescents with depression are indeed effective compared to the control conditions. However, the size of the effects is substantially smaller than the size of the effects found in adults.

One could conclude therefore that the effects are smaller in adolescents compared to those in adults. This difference in effect size is, however, not caused by lower response rates in adolescents who receive therapy, but by higher response rates in the control conditions. Both in adolescents and in adults the response rate (50% symptom reduction from the start to the end of the therapy) is around 40%. The response rate in the control conditions is much higher in adolescent studies (>25%) compared to studies in adults (16-17%).

> *So, when you go into therapy, the chance of getting better is not different between adults and adolescents.*

Only a few therapies have been shown to work

There are only a few types of therapy that have been found to be effective in the treatment of adolescents. In most meta-analyses, in which the results of individual effect sizes are statistically integrated into one estimate of the effects, it is found that cognitive behavior therapy and interpersonal psychotherapy are effective in adolescents:

- Cognitive behavior therapy helps people identify and change unhelpful thought patterns and behaviors that maintain depression, and to replace them with more balanced thinking and healthier, mood-improving actions.
- Interpersonal psychotherapy helps people improve their mood by addressing relationship problems, communication patterns, and major life changes that contribute to or maintain depression.

In a new study that will be published soon, we found that behavioral activation is also effective in the treatment of depression in adolescents. Behavioral activation helps people reduce depression by gradually increasing engagement in meaningful, enjoyable, and goal-directed activities while reducing avoidance and withdrawal.

That is a clear difference with adults, where many more types of therapy have been found to be effective in multiple outcome studies and meta-analyses. This limits the possibilities for adolescents. That is important, because the three therapies are effective compared to control conditions, but that does not mean they work for everyone. As we saw, only about 40% of adolescents respond to therapy. That means that if one therapy does not work, there are only two other options that may work.

What about antidepressants?

Next to psychotherapy, antidepressants can also be a treatment option for depression and anxiety in adolescents. This is, however, not recommended in mild depression. It can be an option in more severe depression, but only in addition to psychotherapy, when that does not work sufficiently. Antidepressants are also not easily recommended, because they may result in a small increase in suicidal thoughts or behaviors early in treatment in some adolescents. Fluoxetine is the medication for which most evidence is available.

In summary

So, yes, treatments of depression in adolescents are effective, but that does not mean they work for everyone. The effects of these treatments are modest, and it

may take effort to get better. The good thing about seeking professional help is not only that these therapies can be provided, but also that clinicians stay with you when a treatment does not work sufficiently, and they will try to help until the adolescent is doing better, even when it takes long.

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CHAPTER 5

Next steps

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What can I do if therapy does not seem to work?

"I am now in therapy for a few months now, but I don't feel I get better. It just feels that the things we discuss are not related to my problems and don't really help me. What should I do? Quit? Discuss it with her? Switch to medication?"

The quiet assumption that therapy always works

Many people suffering from mental health problems think that therapies should work. The same is true for therapists. If a therapy is 'evidence-based' then it should work, they assume. There is, after all, research showing that it works, right?

Unfortunately, that is not always the case. The outcomes of therapy are clearly better than doing nothing, but that does not mean that everyone gets better. For example, in depression it has been estimated that 42% of people receiving therapy improve substantially (their symptoms are half of what they were at the start of therapy), while only 16 to 17 percent improve when they don't get this therapy. In anxiety disorders, PTSD and OCD between 30 and 40% of people improve substantially in therapy.

> *That means that many people receiving therapy do not improve substantially. And if you are in therapy, but you do not improve substantially, you are certainly not an exception.*

So what can you do?

Be realistic—and go easy on yourself

First of all it is important to be realistic about what you can expect from therapies. The therapist should inform you about the chances of getting better when you get the therapy, but therapists are also often not aware that therapies have limited effects. Therefore it is important as a client that you do not expect automatically that it will work for you. If you are lucky it does work right away, but there is a considerable chance that it will not work.

When you are in therapy and after a while you don't think you are improving enough, it is also important to remember that this is not caused by you. It is also not related to the complexity of your problems or your ability to improve. It is just a logical consequence of the limited effects of therapies, and it is not known why some people respond right away and others don't.

Talk to your therapist

But if you do not improve enough it is important to discuss this with your therapist. In many therapies a discussion of how things are going is built in at several points during the therapy, but that is not always the case. So if you feel things are not getting better, you should take the initiative to talk about this with your therapist.

This may be difficult and often you don't want to disappoint the therapist, who is also doing the best they can, or you may feel they will be angry with you. But therapists are trained for this work, including the handling of complications like this. You may expect a professional and constructive attitude from them.

You can then discuss with your therapist about the goals you have for your therapy, what has been working and what not.

What can change?

Maybe you can continue with the current therapy, but change the focus. Or maybe you should get another type of therapy (there are countless types of therapy), maybe you should get another therapist, or maybe you should add medications to the treatment. Maybe the therapist may want to have another diagnostic interview with you, to get a better picture of what exactly is going on.

You are not alone

When you feel that therapy is not working good enough, you are certainly not alone. Many people who recover say afterwards that it took quite a search to find the right treatment by the right person. It is important to keep an open mind when going into therapy, but also to keep a focus on what you need and what is best for you to recover.

Read an interview with me about this subject on the website of Success.

33

Can depression be “treatment-resistant”?

“I regularly see patients with depression who have not improved after trying two different antidepressants and are therefore considered to have treatment-resistant depression. But I also hear a lot of criticism about the term. Is treatment-resistant depression really a different type of depression?”

A term that is not well chosen

Unfortunately, the concept of treatment-resistant depression is not well chosen. It suggests that a patient with treatment-resistant depression has a specific type of depression, which is especially hard to treat compared to a ‘normal’ depression. It suggests that this specific type of depression is something special, with specific characteristics that make it hard, and maybe even impossible, to treat. That is, however, a misconception.

> *The so-called treatment resistance has nothing to do with the depression, but more with the limited effects of available treatments.*

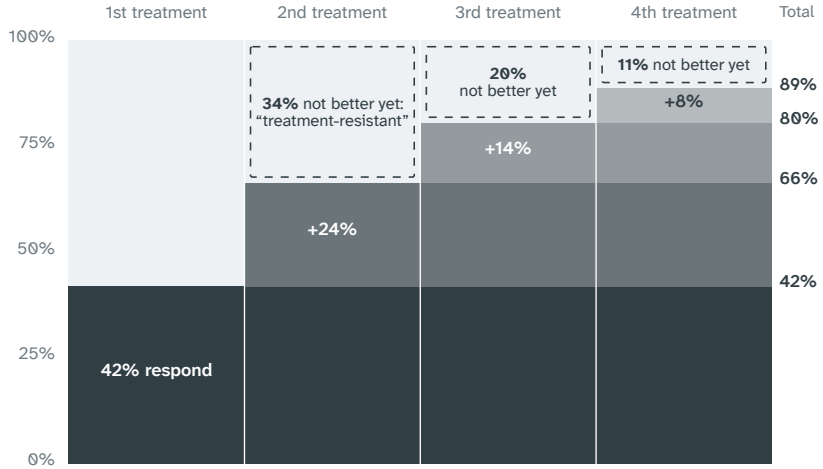
Why so many people meet the definition

Treatment resistance is usually defined as not responding to at least two types of antidepressants. However, in a large meta-analysis in which we integrated the results of more than 200 randomized trials, we found that 42% of patients receiving psychotherapy responded to treatment (response defined as a 50% symptom reduction between the start and the end of the therapy). It is known from many other studies that pharmacotherapy has comparable effects. This means that more than half of the people who get a regular treatment do not respond to the first treatment.

When the remaining 58% of patients get a second treatment, it would be reasonable to expect that again 42% of these 58% respond (or maybe a little less). That would still leave about one third of patients not responding to the first two treatments. All these remaining patients would fit the definition of ‘treatment resistance’.

Why about one in three patients ends up “treatment-resistant”

An illustration with 100 patients: 42% respond to their first treatment. If 42% of those who have not yet responded respond to each next treatment, about one third have still not responded after two treatments—the usual definition of treatment-resistant depression. Many of them still get better with the next treatments.



Illustration, not measured data: assumes that 42% of patients who have not yet responded respond to each next treatment (response = at least 50% symptom reduction; 42% from Cuijpers et al., 2021, Acta Psychiatrica Scandinavica). In reality, later treatments may help somewhat less.

When considered from this perspective, patients can be ‘lucky’ when they respond to the first or second treatment, and ‘less lucky’ when they don’t. That has nothing to do with the depression or with the patient, but more with the limited effects of treatments.

“Difficult-to-treat” is not much better

Some clinicians try to solve the issue by redefining treatment-resistant depression as ‘difficult-to-treat’ depression. But that still suggests that this is a characteristic of the depression, and makes the patient feel as if there is something wrong or difficult about their depression. However, this is not related to the depression, but only to the treatments, which are simply not as effective as everyone would want them to be.

Psychotherapy is left out of the definitions

There is something else problematic about treatment resistance. Definitions of treatment-resistant depression focus almost entirely on antidepressant medica-

tions and largely ignore psychological treatments. One review identified 148 different definitions of treatment resistance, but only six (4%) included failure to respond to psychotherapy.

This is remarkable, because psychotherapy is an effective treatment for depression, and combining psychotherapy with medication is more effective than either treatment alone. The WHO mhGAP treatment guideline recommends not to prescribe antidepressants without psychological treatment. Many patients classified as treatment-resistant have therefore not received all available evidence-based treatments, and if they have only received antidepressants, their treatment has been at least suboptimal.

A better way to talk about it

It would be better to avoid the terms 'treatment-resistant' or 'difficult-to-treat' depression altogether, and to inform patients at the start of the treatment that any available treatment only works for a limited number of patients. They can either be lucky and get better with the first or second treatment, or less lucky and require multiple treatments before they get better. That makes it clear that there is nothing special about the depression, but that non-response is the logical consequence of the limited effects of treatments.

In summary

The term 'treatment-resistant depression' is misleading because it suggests that there is something unusual about the depression itself, while non-response is largely a consequence of the limited effectiveness of available treatments. Instead of labeling patients as treatment-resistant, we should explain that many people need several treatments before they improve.

> *The question should not be why a patient is resistant to treatment, but what we can do next to help them recover.*

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How well does therapy work, and for whom? What makes therapies work, and what makes a good therapist? In this booklet, Pim Cuijpers answers questions from patients and clinicians, drawing on what meta-analytic research tells us about psychological treatments.

Pim Cuijpers with Mathias Harrer



METAPSY



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