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Personalizing behavioral interventions: the case of late-life depression

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SUMMARY

This article reviews the potential utility of behavioral interventions in personalized depression treatment. The paper begins with a definition of personalized treatment, moves to current thinking regarding the various causes of depression, and proposes how those causes can be used to inform the selection of behavioral interventions. Two examples from the late-life depression field will illustrate how a team of researchers at Cornell University (NY, USA) and University of California, San Francisco (CA, USA) created a research partnership to select and study behavioral interventions for older adults with risk factors associated with poor response to selective serotonin reuptake inhibitor medications. The paper ends with a discussion of how the process used by the Cornell University–University of California, San Francisco team can be applied to the selection and development of behavioral interventions for other psychiatric disorders.

Personalizing behavioral interventions for late-life depression

Decades of intervention research have led to the development of effective treatments for major depression across many age groups. Major depression, as defined by the Diagnostic and Statistical Manual, Fourth Edition (DSM-IV) [1], consists of no less than five of nine symptoms being simultaneously present over a 2-week or more period of time. These symptoms include low mood, lack of interest or enjoyment in usual activities, poor appetite, poor sleep, low energy or fatigue, poor concentration, irritability, feelings of worthlessness, and suicidal thoughts or feelings. Major depression is less common in older adults than younger adults [2] but has detrimental health and society effects, including increased medical expenditures, premature death, worse health, poor response to treatment for chronic illness, and increased risk for nursing home placement [3]. Older adults also have the highest completed suicide rates of any age group (adolescents have more attempts), and suicide is unrelated to medical status [4]. Given the pace at which the population is aging globally, clinicians will see many more older patients suffering from depression and will be expected to manage these patients and the negative impact major depression in older adults, also called late-life depression (LLD), has on the health of the older person.

Fortunately, there are very effective treatments for major depression and LLD. The evidence base for medication and behavioral interventions is substantial enough to allow healthcare policy makers to develop treatment guidelines that inform both patients and clinicians about the best practices for treating this disorder [5]. Evidence-based treatment for major

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depression is available for nearly all age groups and ethnic/racial groups [6], and lately many evidence-based treatments are becoming available in a variety of healthcare and social service settings, such as primary care medicine [7], home healthcare [8], schools [9], inpatient medicine [10] and, recently, on the internet [11–13]. Because of the tendency for LLD to be underestimated, for late-life suicide to not be taken seriously by healthcare providers [14], and for older adults to be under-represented in mental health services [15] there have been a number of efforts in place to ensure that evidence-based recognition and treatment of LLD is available in service settings where older people are most likely to seek treatment (e.g., primary care medicine) [7]. Because of the success of these initiatives, these models of depression care integration into primary care medicine are now becoming available for all age groups [16]. Furthermore, there are a variety of intervention types that adults and older adults can chose from, including behavioral (psychotherapy and case management [CM]) and medical (medications and electroconvulsive therapy) interventions. These interventions on average are effective in not only reducing symptoms of major depression [17], but have been found to improve daily functioning [18–21] and in some cases reduce costs associated with disability.

Despite the availability and success of these interventions for treating major depression, ensuring people receive the right evidence-based treatment for their major depression is still complicated. Epidemiologists report that only 40% of people seeking treatment for major depression respond to the first treatment type delivered, whereas the remainder require multiple trial-and-error attempts before they show a response to treatment [22,23] and some fail to respond at all [7,24]. The inability to match people to the best treatment can have significant consequences on overall recovery; trying several ineffective treatments may result in increased clinician and patient pessimism about the potential for change. In addition, the longer it takes to recover, the greater the consequences for patients in terms of prolonged disability and poor quality of life, and reduced productivity. Unfortunately, with the exception of general treatment guidelines that specify the point in the course of major depression one should try psychotherapies, antidepressant medications and electroconvulsive therapy, there is little in the way of guidance for selecting the best intervention for a given individual among treatment types (e.g., when should one try cognitive behavioral therapy (CBT) and when should one try interpersonal therapy? Under what circumstances is problem-solving treatment preferred over behavioral activation?). As a result, there is a strong and steadily growing interest in the development of personalized treatment for major depression to help clinicians select treatments that will result in fast recovery.

Recently, the National Institute of Mental Health in the US (NIMH) embarked on a research agenda to inform personalized treatments of mental illnesses based on exploratory studies of predictors and moderators of treatment response. The NIMH strategic plan and, in particular, the resulting *From Discovery to Cure* report, specifically calls for more research to develop new and better interventions that address the various causes of mental illness [25]. Although the emphasis of this report is on the development of medical and biologically based interventions, the NIMH is quick to point out in the overview to the *From Discovery to Cure* report and the strategic plan, that information from cognitive neuroscience, biology, sociology and psychology can also be used to develop personalized behavioral treatments for mental illnesses. To date a majority of the research on personalized depression treatment has focused on medications and medical technologies; behavioral interventions, such as psychotherapy, have been under-represented in this line of research. Part of the problem is due to the history of personalized treatment, which has its roots in the discovery of genetic markers and their association to treatment response. This focus of personalized treatment research on medically oriented interventions may be short sighted in the case of major

depression; many populations at high risk for major depression (adolescents, older adults and ethnic minorities) indicate a preference for behavioral interventions [26–43].

The purpose of this paper is to discuss and demonstrate the potential utility of behavioral interventions in the development of personalized depression treatment. The paper begins with a discussion of what personalized treatment means, moves to current thinking regarding the various causes of major depression and proposes how those causes can be used to inform the selection of behavioral interventions. The paper uses an example of the work of Cornell University (NY, USA)–University of California, San Francisco (UCSF; CA, USA) research partnership in LLD, and throughout the discussion uses two examples to illustrate how research from neuroscience and social science can inform the personalized selection of behavioral interventions.

Why focus on LLD?

A focus on LLD, an area of research that has historically been undervalued, has considerable potential in helping clinical investigators understand differential response to depression treatments and in turn inform the clinical field about how to select treatments based on clinical features that are predictors of treatment outcome. To be clear, when we talk about LLD, we are not exclusively talking about late-onset depression, a term used to describe a situation when the very first lifetime episode of major depression occurs after the age of 65, we are talking about any major depressive episode that occurs after the age of 65, regardless of the patient's history of major depression. Older adults possess many of the suspected predictors of poor response to depression treatment, particularly antidepressant medications. For instance, deficits in cognitive functioning, medical comorbidities, disability, social isolation and poverty are all thought to be potential predictors to antidepressant treatment response. As will be made clearer in this review, indeed, research on older peoples' response to antidepressant medication finds that memory impairment [44], increased disability and medical burden [45,46], and executive dysfunction [47] are predictors of poor response to antidepressant treatment. Although age of first episode (before or after the age of 65) has historically been a predictor of interest, experts in geriatric mental health now realize that age of onset alone is a poorly defined predictor, as late onset could be due to onset of disability, cognitive decline, increased social isolation and financial strain. Early onset as a predictor is also confounded by other variables, such as number of previous episodes. Furthermore, in order to understand response to depression treatment, investigators must also be able to explore the various causes of major depression symptoms, and older adults are more likely to have different etiologies for their depression; LLD, regardless of onset, can arise as a function of neurological disorders such as stroke, Parkinson's disease and Alzheimer's disease; however, LLD can also arise as a function of social losses, financial strain and isolation. The capacity to explore differential treatment response in a population with so diverse a presentation and etiology of major depression yields incredible potential for understanding treatment response in major depression across all populations and age groups.

Definition & explanation of personalized treatment

Personalized treatment (sometimes referred to as targeted treatment) has its roots in the movement in medicine to customize healthcare to individuals based on clinical presentations of specific illnesses. According to this tradition, within each diagnosis there will be variation between individuals with an illness that has the potential to effect treatment decisions. In the context of mental health, personalized treatment has mainly involved the systematic use of genetic, neurological, biological and sociological information about an individual patient to optimize patient care [25,48]. The movement toward personalized treatment is in part a

reaction to decades of research that has focused on epidemiologically informed recommendations based on data from large cohorts of patients, as well as the efficacy-based clinical trial discipline that, while very useful for determining general risk factors for diseases and aggregated response to treatment, have been unable to account for individual variability to treatment based on biological and environmental variations of individuals within a diagnostic group.

As an example of this thinking, the Weill Cornell Institute of Geriatric Psychiatry proposed a biopsychosocial model that could be used to inform the personalization of treatment for LLD [47]. This model suggests, based on previous research into the risk factors for developing LLD, that at least three risk factors are related to the development of LLD: age and disease-related factors (e.g., arteriosclerosis) that affect the integrity of neural networks, particularly the frontostriatal pathways and important brain structures (i.e., amygdala and hippocampus); genetic vulnerabilities; and psychosocial adversity (e.g., poverty, disability, familial stress). Any or all of these risks for LLD could influence response to treatment and as a result could constitute a target for personalized treatments. For instance, interventions that compensate or remediate neural network deficits (e.g., plasticity-based interventions, such as computerized remediation programs [49] or strategy-based remediation programs [50]) may be best suited for older adults who present with LLD and comorbid vascular disease, while interventions that address poverty-related adversity (e.g., clinical CM and supportive therapy) may be better suited for older adults who are depressed because of their social circumstances. In order to determine if these risk factors for LLD are useful in treatment personalization, however, research to study how these factors influence treatment outcomes needs to be conducted first.

Methodological approaches to informing personalized treatment: predictors of treatment outcome

According to the NIMH strategic plan, personalization of depression interventions should be informed by clinical trials focusing on biological, genetic, behavioral, psychological and environmental predictors and moderators of treatment effectiveness in different populations [25]. Predictors are variables associated with treatment response that are usually present before treatment begins and are not associated with the treatment assignment. An example of a treatment predictor of major depression treatment outcomes is the co-existence of anxiety symptoms. In LLD, for example, the presence of generalized anxiety symptoms does not appear to predict response to medication and behavioral treatments, but symptoms related to post-traumatic stress disorder do; however, as yet, we do not know if people with LLD and post-traumatic symptoms respond better to medication treatment or behavioral treatment. All we know is that, in general, people with this comorbid presentation of LLD will have worse treatment outcomes than those who do not [51]. When a variable predicts treatment outcomes, all we know is that people who possess the predicting variable will have a positive or negative response to a particular treatment. What we do not know at this point is whether people who possess the risk factor will respond better to one treatment than they will to another [52].

Biological predictors of LLD

In the area of LLD there has been research that has successfully identified predictors of response to antidepressant medications. While memory impairment, age of onset and disease-related onset are predictors of response to antidepressant medication, of particular interest to the geriatric psychiatry field has been the role that executive functions play in treatment response. To be very clear here, when we talk about impairments in the executive functions, we do not mean to talk about incipient dementia, but rather, a set of behaviors that

all people with mental illnesses possess, particularly people with mood disorders [53–55], attention deficit disorders [56] and schizophrenia [57]. In this context, executive dysfunction is defined as a set of behaviors that cut across mental illness domains, specifically apathy, poor attention, distractibility, disinhibition or the opposite, inhibition, and poor planning/complications with goal-directed behavior. Research is beginning to show that the more severe the executive syndrome is, the less responsive patients are to existing treatments [58–61]. Furthermore, across disorders, different symptoms within the executive syndrome have differential prominence as a predictor of treatment outcome. Although our focus here is on LLD, when we talk about executive dysfunction, we mean the executive syndrome that is associated with major depression, not dementia (although a proportion of those with both LLD and executive dysfunction may convert to dementia in the future).

Investigators at Cornell University who were interested in untangling poor response to selective serotonin reuptake inhibitor medication in older adults found that older adults with poor or unstable response to e-citalopram exhibited a specific clinical presentation distinct from those who responded well to this treatment [62]. Specifically, researchers at Cornell University observed, and other investigators confirmed, that older adults exhibiting apathy, trouble making decisions and difficulty initiating goal-directed behavior were less likely to respond to e-citalopram [63]. These behaviors were noted to be similar to patients who exhibit executive dysfunction, as we described above. This observation generated a hypothesis about the potential neurological underpinnings of this behavior, in particular the role that diminished executive functions have on capacity to respond to anti depressant medications. Using neuropsychological tests of executive functions, investigators studied the link between this particular presentation of depression, performance on neuropsychological tests of executive function and response to antidepressant treatment. In a series of these studies, researchers found that poor performance on the Stroop Color Word Test (a test that is also known to be associated with information processing speed) and the initiation and perseveration subscale of the Mattis Dementia Rating Scale were also associated with poor response to antidepressants [44,62,63]. It is important to note here that the scores that correlated with treatment outcome were not age-adjusted scores, further highlighting that what we were investigating was not an incipient dementia, but a correlate of mental illness. The investigators of these studies are quick to point out that while many of the patients with combined major depression and executive dysfunction are at risk for developing dementia, these patients do not have dementia, and the executive dysfunction exhibited in these patients is related to their major depression and how they experience the syndrome [64]. In short, these investigators found that executive dysfunction, as measured by poor Stroop performance, is a predictor of response to e-citalopram.

Psychosocial predictors of response to treatment in LLD

Not all predictors need to be biological to inform personalized treatment. As pointed out in the Cornell model, social adversity may also be a potential moderator of treatment outcome. The Over-60 Program in the University of California, San Francisco's Depression Center (a member of the National Network of Depression Centers) has conducted research on the behavioral treatment of LLD in low-income communities and has found that standard behavioral interventions, such as CBT, may not be as effective in low-income communities as they are in middle-income communities of older adults. The first study to inform the potential moderating effects of poverty on treatment of LLD found that although older, low-income elderly showed an initial response to CBT, the average depression symptoms were still higher in these communities than in those found in middle-income communities; average Hamilton Depression Scale scores in the poverty samples post-treatment are 12 [65], whereas average Hamilton Scale scores in middle-income samples are five [66]. A qualitative exploration of the utility of cognitive behavioral treatments for this population

revealed that while cognitive behavioral treatment was acceptable to many patients, everyday struggles related to poverty (e.g., urban crime, insufficient access to nutrition and concerns over bills) made the application of this intervention into daily life complex. The Over-60 team determined that the stress related to poverty status predicts the effects of CBT in older adults.

Using predictors to select treatment & identify potential moderators

Moderators are pretreatment characteristics not associated with treatment assignment that are differentially associated with treatment outcome [67–69]. Although research on predictors of treatment outcome will narrow the field of candidate moderators down to the most likely candidates, not all predictors will be moderators. People with LLD and symptoms of post-traumatic stress may have equally poor outcomes regardless of the treatment used. Although knowing the predictors of treatment outcome is an important step in the personalization of treatment, the identification of a treatment moderator is critical in personalizing treatments. Once moderators are identified, we are in a better position to know from the outset which treatments are best for certain presentations of major depression.

Behavioral interventions have an important role in this research, however, to date there are very few studies or examples of how behavioral interventions have been used to address biological and environmental predictors of treatment outcomes. Two studies using behavioral interventions to address predictors of LLD treatment, one addressing predictors to medication treatment and one addressing predictors of psychotherapy, illustrate the potential behavioral interventions have in personalized treatment.

Behavioral interventions targeting moderators of antidepressant medication outcomes in LLD

The Collaborative Psychotherapy study for Executive Dysfunction and Depression (COPED) [18,70] is an excellent example of the discovery of a biological predictor of the effects of antidepressant medication that led to the selection of a behavioral treatment as a potentially useful alternative to e-citalopram for individuals with an executive presentation of LLD. The discovery of executive dysfunction as a predictor could have led the Cornell team to explore medical augmentations, or even plasticity interventions, as a means of enhancing treatment response to medications. While these are viable options, the research then – and now – on the effects of other psychiatric medications on executive impairment and the utility of plasticity interventions in mental illness is very limited. Fortunately, problem solving therapy (PST) [71,72] had recently been found to be an effective treatment for LLD in a number of clinical trials [66,73] and, based on its theory and strategies, appears to directly target some of the critical symptoms the Cornell group found to predict poor response to antidepressant medication (i.e., apathy, difficulties making decisions and difficulty initiating goal-directed behavior).

Problem solving treatment is a 12-week intervention that consists of three treatment phases: phase one lasting 3 weeks is psychoeducational, helping participants understand the problem solving steps and using the problem solving action planner for working on psychosocial problems; phase two (weeks 4–10) consists of independent practice of the PST skills; and phase three (weeks 11 and 12) consists of two relapse prevention sessions, using the problem solving model to develop plans to maintain depression and functional treatment gains. PST itself consists of a seven-step process to solve problems. These include problem orientation, which directs patient attention to one problem at a time; problem definition, which helps patients select our relevant information to determine what the root problem is in a given situation; goal setting, which focuses attention to the desired outcome; brainstorming, which helps patients consider multiple methods for reaching the goal;

decision-making, a method employed to evaluate the alternative solution's likelihood of reaching the stated goal and picking the best solution among the choices; and action planning, which involves a step-by-step plan for the patient to implement his/her solution. PST was compared with supportive therapy, which served as an active attention control with some evidence for its effectiveness in older adults with major depression [74].

Two hundred and twenty two people over the age of 60 were randomized to receive PST or supportive therapy (ST). Participants met criteria for major depression and deficits in cognitive conflict, assessed via the Stroop Color Word Task. All received 12 weeks of psychotherapy and were followed for 9 months from baseline assessment. We were able to demonstrate that both PST and ST were effective interventions for treating LLD in this population, and that PST was significantly more effective than ST in depression and disability outcomes [18,70]. It is important to note here that while PST was superior to ST in this trial, even ST could be a better treatment choice for older adults with executive dysfunction. As was discussed in the original paper, both interventions resulted in substantially more numbers of treated individuals than are treated in late-life antidepressant medication studies [70]. Thus far, the results from these studies seem to indicate that in patients with LLD and executive dysfunction, among the treatment options available, PST is the most likely to result in a positive treatment outcome from the outset, but that ST could be a viable alternative to antidepressant medications as well, should clinicians trained to deliver PST not be available.

Although the results of this study, coupled with research from the antidepressant field, has been useful in personalizing treatment decisions related to LLD, and that executive dysfunction is a likely moderator of treatment response, this data still does not prove that executive dysfunction is a confirmed moderator of treatment response. In order to determine moderation, the next step would be to conduct a study recruiting depressed older adults with and without executive dysfunction, and then randomize the sample to receive antidepressant medication or PST. Clinically, this research suggests that when clinicians are working with older adults with LLD and see executive impairments, their first choice of treatment may be problem solving treatment instead of an selective serotonin reuptake inhibitor medication.

Behavioral interventions addressing predictors of psychotherapy outcomes in LLD

As mentioned earlier, the Over-60 Program has identified that psychotherapies known to be effective in treating LLD, as well as major depression in younger, low-income communities (in this case, CBT) are not as effective in treating major depression in low-income older adults [65] and that the likely reasons for this are the difficulties low-income older people have in accessing social services that could address their poverty-related needs. In the Psychotherapy Effectiveness Project for Underserved Populations study (PEP-UP) [75], the Over-60 program studied the impact that clinical CM would have as a standalone treatment and as an adjunct to CBT.

Clinical CM is a term that encompasses a number of social strategies to help people in distress obtain social assistance and services. The most common models of CM are reviewed in [76–79]. Previous studies have demonstrated that CM has been found to be effective in older adults. CM for older adults with medical illnesses [80] and for nursing home residents [81] has resulted in both better adherence to psychotherapy and reduction of depressive symptoms [82–84]. The Over-60 team felt that this intervention could act as an enhancement to CBT by encouraging patients to use the CBT techniques while simultaneously addressing the service needs of the older adult.

The purpose of the PEP-UP study was to determine the value added by providing clinical CM to CBT. The sample was recruited from an urban hospital serving low-income and

uninsured patients. We were particularly interested in recruiting people over the age of 59 with income levels below US$15,000 a year and who met DSM-IV criteria for major depression. Depression severity was assessed at baseline, 16 weeks (treatment end) and 6 months after completion of treatment. CBT appeared to be ineffective. By treatment end, a time-by-treatment interaction was found in that participants treated with CM had greater reduction in depressive symptoms than participants treated with CBT alone or CM–CBT. The time-by-treatment interaction remained 6 months after treatment ended, in that CM and CM–CBT had better outcomes than CBT alone. These observations suggest that CM alone and in combination with CBT are superior to CBT alone in reducing depressive symptoms in low-income elders with major depression.

As discussed above in the PST study, although clinicians can use this information to personalize treatment options for older adults with LLD, poverty has still not been proven to be a moderator of treatment. To determine that CM–CBT is truly the best option for older adults with low incomes, and not simply a better intervention than CBT alone in treating anyone with LLD, one would need to conduct a randomized trial that included older adults of all incomes and demonstrate that differential treatment response between CBT and CM–CBT was evident in the low-income group only. From a clinical perspective, however, this study suggests that behavioral interventions alone may be insufficient for treating LLD in low-income communities, and that clinical CM may be a necessary adjunct. A recent interesting study also found that low-income adults with LLD also do not respond well to antidepressant medications [85].

Future directions for the personalization of behavioral interventions for major depression

The COPED and PEP-UP studies are but one example of how behavioral interventions can play an important role in the personalization of major depression treatment, based on both biological and environmental risk factors for poor response to antidepressant treatment. Several studies have begun to explore the role that other clinical characteristics have on the effects of treatment for major depression. Thus far, major depression characterized by rumination [86,87], affective dysregulation [88,89] and negativity biases [90], have been identified as predictors of poor response to both medication and psychosocial treatments. As an example, the UCSF site of the National Network of Depression Centers is conducting research to determine the effect that mindfulness-based cognitive therapy has on depressed patients with excessive rumination symptoms [91,92]. Additionally, work at Cornell University has further explored executive function as a predictor of poor antidepressant outcomes and have isolated a particular neural network, the cognitive conflict network, as an important predictor of treatment outcome. The UCSF and Cornell team are beginning to investigate whether plasticity-based interventions known to activate that network in older adults is as effective as PST in treating LLD.

Future perspective

Although the mandate for the development of personalized treatments for mental illnesses has been handed down to investigators of all types, the future of personalized treatment development for mental disorders in the next 5–10 years is unclear. Unfortunately, we know very little about the predictors and moderators of treatment outcomes in LLD, nor has there been any research on how known predictors interact to influence outcomes, and good studies to uncover predictors and moderators tend to be large and expensive, a challenge in a time when dollars to support clinical research are dwindling. There are, however, a couple of avenues that we can take to expedite the discovery of treatment predictors and moderators to inform the personalization of depression treatment. Information available in existing health

system databases could lead to potential indicators for treatment innovations, and the integration of biological, behavioral, environmental, cultural and health information in studies of risk factors could narrow down candidate mechanisms – this method would also allow for much better understanding of how biological markers interact with environmental or sociological factors that may or may not influence treatment response. A challenge to large-scale investigation of treatment predictors is that certain basic science methods are difficult to employ on a large scale, however, with advances from groups like the Alzheimer's Disease Neuroimaging Initiative, which is developing methods for combining and processing MRI data from different centers, the potential for methodological integration is on the horizon. A second approach to expedite the identification of predictors and moderators of treatment response, and subsequently the personalization of depression treatment, is the development of shared research databanks that are beginning to emerge that would allow investigators opportunities to conduct exploratory analyses on samples sizes that would normally be unattainable from one research site. One example of a shared research site is BRAINnet.net, which currently includes data from neurological studies of mental illness and treatment response across 20 countries, which has resulted in over 200 publications. The National Network of Depression Centers is an emerging research collaborative of over 20 universities working together to use the same baseline and outcome measures. Collaborations such as these should provide ample data for personalized treatment of depression. Finally, a team-based approach to research will move the field toward personalized treatment of major depression much faster than investing heavily in one arm of science. Innovations in health and technology have benefited greatly from a team science approach. Science of Team Science intentionally brings experts from different fields to examine the same problem in an effort to create scientific and technological innovations and to answer research questions about particular phenomena. White papers such as the *From Discovery to Cure* report are excellent first steps in that direction; examples of how this area of work can inform the personalization of behavioral interventions for major depression, such as the ones presented in this review, need to be broadly disseminated to stimulate others to invest in this important line of research.

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Practice points

Although most treatments for depression are in general effective, many patients do not respond to the first treatment they try.

Personalized treatment involves collecting clinical information from patients about known predictors to treatment response, and selecting interventions based on whether the patient possesses any of those predictors. As an example, an older person who has major depression and complains of significant apathy, problems making decisions and trouble getting started on tasks may not respond well to selective serotonin reuptake inhibitor medications and may instead respond best to problem-solving treatment.

It is assumed that identifying predictors of treatment response, and eventually moderators of response, will give clinicians more power to match patients to the best treatments for their condition, which in turn should result in quicker recovery from major depression.

In the future, clinicians will see more and more information about predictors of treatment response, which should help with treatment selection. Unfortunately, there has not been as much research begun on predictors of outcomes to behavioral interventions, like psychotherapy.

Late-life depression (i.e., major depression in people over the age of 65) holds considerable promise as an avenue of exploration into predictors of treatment response. This population possesses many of the suspected biological and psychosocial predictors of treatment response. This is not to say that all older adults are sick, demented, disabled, lonely and poor; rather, the base rates for these conditions are higher among older adults than in other populations, and as such this population provides researchers an opportunity to understand how these suspected predictors impact treatment outcomes individually and comorbidly.

Globally, the population of people over the age of 65 years is growing rapidly, and although major depression is not necessarily a common disorder, by sheer volume, clinicians will see their practices begin to age. Information about the best treatments for this age group is important to obtain. A particular emphasis in this research should focus on behavioral interventions, as older adults prefer these treatments.

Currently, suspected predictors of antidepressant treatment in late-life depression are: memory impairment, age of first episode, comorbid anxiety symptoms, executive dysfunction and poverty. Less is known about predictors of behavioral intervention outcomes, although poverty seems to predict the success of cognitive behavioral therapy in older adults.

Clinical case management appears to be a useful adjunct to behavioral interventions for late-life depression in low-income older adults. Problem solving treatment appears to be an effective treatment alternative for older adults who have symptoms of executive dysfunction.