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Psychosocial and pharmacological interventions for depressed adults in primary care: A critical review

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Abstract

Primary care settings are the principal context for treating clinical depression, with researchers beginning to explore the efficacy of psychosocial and pharmacological treatments for depression within this infrastructure. Feasibility and process variables also are being assessed, including issues of cost-effectiveness, viability of collaborative care models, predictors of treatment outcome, and effectiveness of treatment providers without specialized mental health training. The Agency for Health Care Policy and Research and American Psychiatric Association initially released guidelines for the treatment of depression in primary care [American Psychiatric Association, 1993. Practice Guidelines for major depressive disorder in adults. American Journal of Psychiatry, 150, 1–26., American Psychiatric Association, 2000. Practice Guideline for the treatment of patients with major depressive disorder (revision). American Journal of Psychiatry, 157, 1–45], however, a vast literature has accumulated over the past several years, calling for a systematic re-evaluation of the status of depression treatment in primary care. The present study provides a contemporary review of outcome data for psychosocial and pharmacological interventions in primary care and extends beyond AHCPR guidelines insofar as focusing on feasibility and process variables, including the training and proficiency of primary care treatment providers, cost-effectiveness of primary care interventions, and predictors of treatment response and relapse. Based on current guidelines, problem-solving therapy (PST-PC), interpersonal psychotherapy, and pharmacotherapy would be considered efficacious interventions for major depression, with cognitive–behavioral and cognitive therapy considered possibly efficacious. Psychotherapy and pharmacotherapy generally are of comparable efficacy, and both modalities are superior to usual care in treating depression. Methodological limitations and directions for future research are discussed.

Contents

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The National Comorbidity Survey suggests a lifetime prevalence of 17% and 1-year prevalence of 10% for major depression (Kessler et al., 1996). Within primary care, and mindful of data indicating that clinical depression is largely unrecognized in this context, approximately 10–30% of patients present with a depressive disorder (McQuaid, Stein, Laffaye, & McCahill, 1999; Stein, Kirk, Prabhu, Grott, & Terepa, 1995). Functional impairment associated with depression is extensive, including exacerbation of medical illness and impact on physical health (Spiegel & Giese-Davis, 2003; Stevens, Merikangas, & Merikangas, 1995), maladaptive cognitive processes (Beck, Rush, Shaw, & Emory, 1979), decreased positive behaviors (Hopko, Armento, Chambers, Cantu, & Lejuez, 2003; Lewinsohn, 1974), and problems within social relationships (Klerman, Weissman, Rounsaville, & Chevron, 1984). Major depression also is highly comorbid with anxiety disorders and alcohol abuse (Mineka, Watson, & Clark, 1998), and the economic cost of depression is staggering, with estimates approaching several billion dollars per year (Wang, Simon, & Kessler, 2003). Much of this economic burden comes in the form of job absenteeism and decreased job performance and productivity (Lerner et al., 2004; Zhang, Rost, Fortney, & Smith, 1999). In fact, patients who are successfully treated for their depression are more likely to maintain paid employment and have fewer missed days of work (Simon et al., 2000).

Over the past decade, primary care physicians have emerged as the predominant mental health care providers insofar as diagnosing and treating depression, with the majority of patients with mood disorders receiving treatment in a primary care setting (Norquist & Regier, 1996; Weilburg et al., 2003). Of those patients treated for depression in primary care settings, certain clinical and demographic features seem to be linked with the likelihood of receiving depression interventions. For example, individuals with more severe symptoms of depression, longer duration of depression, more comorbid medical problems, greater functional impairment, cognitive impairment, decreased social support, being female, and those living in urban areas are more likely to receive treatment for depression in primary care (Friedman, Conwell, & Delavan, 2007; Lesser et al., 2005).

Although historically there has been poor recognition of depression symptoms in primary care patients (McQuaid et al., 1999), improved screening procedures have been somewhat useful in addressing this problem (Coyne, Thompson, Klinkman, & Nease, 2002; Rost, Nutting, Smith, & Werner, 2000). While the trend toward improved recognition of depression in primary care is encouraging, improved detection has not necessarily facilitated the use of effective treatment options. For example, Sherbourne et al. (2004) demonstrated that although primary care interventions for depression significantly reduce symptoms in approximately 50% of patients, other studies show that as many as two-thirds of those treated remain symptomatic at long-term follow-up (Mulrow et al., 1998; Magruder-Habib, Zung, & Feussner, 1990). Of equal concern, quality of care for depression as reported by primary care patients is moderate to low (Coyne et al., 2002; Schulberg et al., 1997; Wells, Schoenbaum, Unutzer, Lagomasino, & Rubenstein, 1999), with *quality of care* defined as the capacity of the elements of primary care contexts (i.e. personnel, resources) to facilitate legitimate psychiatric improvement in patients. Indeed, it has been demonstrated that individuals treated for depression in psychiatric settings exhibit greater improvement than those treated in primary care (Coyne, Klinkman, Gallo, & Schwenk, 1997; Coyne et al., 2002; Schulberg et al., 1997).

Given these circumstances, the need to focus on quality improvement is highlighted as a pressing need (Croyle & Rowland, 2003; Schoenbaum et al., 2001; Wells et al., 1999). Efforts toward improving primary care interventions for depression have been made over recent decades and are summarized in treatment guidelines by the Agency for Health Care Policy and Research and the American Psychiatric Association (AHCPR, 1993; APA, 2000; Fochtmann & Gelenberg, 2005). Although these guidelines have been critiqued on various accounts (Munoz, Hollon, McGrath, Rehm, & VandenBos, 1994; Nathan, 1998; Persons, Thase, & Christoph, 1996; Schulberg, Katon, Simon, & Rush, 1998;

Schulberg, Pilkonis, & Houck, 1998), they did represent an advancement toward understanding obstacles involved in treating depression in primary care and provided an algorithm to be followed when treating depressed primary care patients (i.e., pharmacotherapy as a first-line intervention). Several primary issues remained unresolved in the AHCPR guidelines, however, including the extent to which efficacious depression interventions (as demonstrated in traditional contexts) would generalize to primary care, particularly given the heterogeneous nature of primary care patients in terms of demographic, medical, and psychiatric characteristics (Coyne et al., 2002; Schulberg & Rush, 1994; Schulberg, Katon et al., 1998; Schulberg, Pilkonis et al., 1998). Other essential issues requiring further empirical attention included a more detailed account of specific depression interventions and their relative feasibility, efficacy, and effectiveness in primary care settings, who was qualified to provide these interventions, which patient characteristics were associated with treatment success and relapse, and how patient treatment needs could be accommodated in a cost-effective manner?

Over the past decade, in addition to a rapidly growing literature on the efficacy and effectiveness of primary care interventions, researchers have more extensively focused on these central issues. Accordingly, the AHCPR and APA recommendations (1993, 2000) may be somewhat obsolete in that a significant body of primary care research has accumulated that requires assimilation and critique. In addition, although evidence-based reviews exploring depression interventions in primary care have been conducted, these reviews often are relevant to only a subgroup of primary care patients such as older adults (Skultety & Zeiss, 2006). With the objective of promoting a current and comprehensive understanding of primary care interventions for depression and directions for future research, this paper addresses the aforementioned questions with the objective of better addressing the psychological needs of a growing and diverse primary care patient population. We begin by presenting and evaluating primary care treatment outcome data, which is followed by an analysis of predictors of treatment response, assessment of primary care treatment providers, and a discussion of cost-effectiveness issues. As with the AHCPR and APA guidelines (1993, 2000), due to the diverse manner in which researchers have reported findings and the tremendous range of assessment methods and patient samples (i.e., mild self-reported depression, dysthymia, major depression), we update and critique the current knowledge base without conducting formal meta-analyses.

1. Psychosocial and pharmacological treatments in primary care: literature review process

Several clinical trials conducted in primary care have explored the efficacy of psychotherapy, pharmacotherapy, and usual care, generally as these interventions relate to other psychological or medical treatments or wait-list and placebo control groups. Within these studies, "usual care" generally refers to study conditions in which a medical provider's typical course of treatment is provided without influence or provision of additional treatment elements. Along with various pharmacological agents, these trials primarily have involved problem-solving therapy, cognitive–behavior therapy, interpersonal therapy, and/or supportive counseling, with all but the latter approach considered efficacious treatments for clinical depression (APA, 2000; DeRubeis & Crits-Christoph, 1998). All of these therapeutic approaches were considered in the present review, and the initial selection criteria for determining which studies to include were a PsychInfo (2317 hits) and Medline search (3493 hits), whereby *primary care* and *depression* were entered as search terms.

Because of the vast number of primary care studies in which depression has been studied and the differential manner in which the depression construct has been assessed (e.g., as an outcome variable, mediator or moderator of other variable relationships, epiphenomenona of other observations), the literature meeting these initial criteria was quite varied in methodology and focus. Without being overly restrictive, the decision was made to include studies that either directly examined the efficacy or effectiveness of a particular psychotherapeutic or pharmacological intervention or examined an associated feature of implementing these interventions within primary care (e.g., qualifications of treatment provider, cost-effectiveness).

To be as comprehensive as possible, reviewed studies also did not have to include a randomized control trial (RCT) research design. However, primary prevention strategies that involved proactively providing psychotherapy to decrease the likelihood of developing a future mood disorder were not included. Additionally, studies were included that focused on samples of depressed individuals in which patients either met diagnostic criteria for major depression or dysthymia or exhibited substantial though undiagnosed depressive symptoms as assessed via self-report or clinician-administered assessment instruments.

This initial literature review on the two search engines was independently conducted by both authors of this manuscript. Although no formal reliability analyses (i.e., Kappa coefficients) were computed, the two authors discussed which articles to include and formed a consensus decision based on the aforementioned guidelines. In total, 49

intervention studies (published between 1981–2006) and 13 cost-effectiveness studies (published between 1997–2006) were included in the review. Of the 49 intervention strategies, the majority were randomized-controlled trials ($n=41$) and a few were either open clinical trials ($n=5$) or meta-analyses ($n=3$). The primary psychosocial and pharmacological interventions are independently discussed and evaluated below (presented in Appendix Table 1), with latter sections addressing core issues as integrated across interventions (e.g., effectiveness of treatment providers, cost-effectiveness).

1.1. Problem-solving therapy

Problem-Solving Therapy for Primary Care (PST-PC) has been shown to be a promising intervention in primary care, with treatment typically involving an initial 60-min session followed by five 30-min sessions. PST-PC largely is based on research suggesting that a range of life events or problems have a strong association with psychological functioning (Nezu, 1987). PST-PC therefore was designed to attenuate depressive symptoms by assisting patients in generating and developing skills that alleviate life events or problems that interfere with psychosocial functioning (Hegel, 2000). As reported in Appendix Table 1, several studies have supported the effectiveness of PST-PC in a primary care setting, particularly via data supporting comparable effectiveness with various pharmacological interventions (Katon, Unutzer, & Simon, 2004; Mynors-Wallis et al., 2000; Mynors-Wallis et al., 1995). For example, Mynors-Wallis et al. (1995) examined the outcome of patients receiving PST-PC compared to those treated with amitriptyline versus placebo (control). General practitioners provided PST-PC and each of the three treatment groups received similar contact time, with patients in the medication and placebo groups receiving general support and encouragement in place of PST-PC treatment components. Results supported the effectiveness of PST-PC compared to placebo (60% recovery in the psychotherapy group compared to 27% in the placebo control group). No significant difference was found between patients treated with medication relative to psychotherapy (recovery rates 52% and 60%, respectively).

In terms of examining the effectiveness of PST-PC among individuals with minor depression and dysthymia, although one study revealed that PST-PC was not more effective than placebo in reducing dysthymic symptoms (Williams et al., 2000), two other investigations have yielded promising findings (Barrett et al., 2001; Hegel, Barrett, Cornell, & Oxman, 2002). For example, although placebo response was somewhat elevated at 44%, PST-PC was shown to substantially reduce depressive symptoms among patients presenting with dysthymia (57% remission) and minor depression (65% remission) (Barrett et al., 2001). Among individuals with dysthymia, PST-PC was substantially more effective than placebo, but not as effective as treatment with paroxetine (80% remission). Among individuals with minor depression, rate of remission in the PST-PC group was similar to that of placebo and pharmacotherapy, suggesting that patients with minor depression may benefit less from PST-PC than those diagnosed with dysthymia.

Additional studies of PST-PC have assessed the feasibility of having medical personnel provide the intervention, including nurses and primary care physicians (Katon et al., 2004; Mynors-Wallis et al., 1995, 2000; Mynors-Wallis et al., 1997). In the pioneering study to address this issue, Mynors-Wallis and colleagues (1995) examined whether psychiatrists and general practitioners could be trained to effectively provide PST-PC. Data revealed that patients with major depression ($n=91$) exhibited similar treatment outcome and (high) patient satisfaction in both treatment conditions (i.e., PST-PC and Amitryptyline). In a more recent study, family medicine residents underwent a brief PST-PC training program (Hegel, Dietrich, Seville & Jordan, 2004). Upon completion of training, residents demonstrated competence in their ability to provide the treatment, and at three years post-training, 90% of physicians reported that they continued to use the intervention in practice. In addition to physician provision of PST-PC, other researchers have demonstrated that community nurses can be trained to provide PST-PC in primary care (Katon et al., 2004; Mynors-Wallis et al. 1997, 2000). Somewhat antagonistic to these findings, however, another study of primary care patients with minor depression or dysthymia indicated that therapist expertise was a significant predictor of treatment outcome (Hegel et al., 2002).

PST-PC within primary care generally appears to be an effective treatment strategy for depressive disorders and has several benefits over alternative treatments. First, the time and expertise required to provide the treatment is limited relative to other psychotherapeutic interventions studied in the literature (e.g., Schulberg, Katon et al., 1998; Schulberg, Pilkonis et al., 1998; Teasdale et al., 1984). Second, skills learned by patients undergoing PST-PC may prevent future relapse, a benefit over pharmacological treatments in which relapse more frequently occurs following treatment discontinuation (Gatalan et al., 1991; Munoz et al., 1994). Third, several studies support the portability of the treatment in that various medical professionals can effectively provide the intervention (e.g., Katon et al., 2004; Mynors-Wallis

et al., 1997, 2000). Fourth, a growing literature suggests that psychosocial interventions such as PST-PC may be preferred over pharmacological treatments (Priest, Vize, Roberts, & Tylee, 1996; Zeiss & Thompson, 2003).

Although available data indicate the potential effectiveness and feasibility of PST in primary care, the intervention also may involve increased logistical demands with respect to the training and availability of service providers as well as possible increases in health care costs. Considering the relatively similar rate of treatment response among individuals treated with antidepressants versus PST-PC, although more outcome data must be generated, pharmacotherapy may be a preferred initial treatment strategy, with PST-PC being an alternative intervention for non-responders or individuals who prefer psychotherapy over pharmacotherapy. Both PST-PC and pharmacotherapy generally are superior to usual care and placebo conditions, although more RCT's are needed to assess effect sizes and an optimal treatment algorithm. Efficacy of both interventions in relation to depression severity also requires further investigation.

1.2. Cognitive therapy

Empirical evidence for the use of cognitive therapy in primary care is limited, with preliminary studies yielding modest support (Appendix Table 1). Initial studies assessed the feasibility and acceptability of the treatment in primary care using small sample sizes (Scott et al., 1994; Fennell & Teasdale, 1982) whereas other studies involved larger patient samples from a wider range of primary care clinics (Scott et al., 1997; Teasdale et al., 1984). These studies generally suggested that cognitive therapy (CT) might have therapeutic value when provided as an adjunctive intervention to treatment as usual, although longer-term assessment of treatment gains remains relatively unexplored and at this stage is unsupported. For example, Teasdale et al. (1984) demonstrated that individuals receiving a 20-session CT intervention (in addition to usual care) had fewer depressive symptoms at post-treatment as assessed by psychiatrist ratings and self-report. These treatment gains were not maintained at three months post-treatment, however, primarily due to decreased depressive symptoms in the control group. Although the initial treatment gains of CT are noteworthy, use of this intervention requires a substantial number of treatment sessions and considerable expertise to administer, factors that may limit its feasibility.

In response to the former issue, Scott et al. (1997) created Brief Cognitive Therapy (BCT) that consisted of six 30-min sessions provided by an experienced clinical psychologist. A randomized controlled trial examined the potential advantages of supplementing treatment as usual with BCT. Individuals who received BCT in addition to usual care showed significant improvements as indexed by decreased depressive symptoms at all assessment periods and fewer relapses compared to individuals receiving usual care alone. Although BCT addresses the issue of time efficiency, it is notable that psychologists who administered the BCT intervention reported increased difficulty relative to provision of traditional CT (Beck et al., 1979). This issue clearly raises concerns insofar as training medical professionals to administer the intervention in primary care, although as discussed shortly, depression health specialists or physician extenders might be useful in fulfilling this role.

In conclusion, only minimal research has explored the utility of cognitive interventions in primary care, likely due to inherent limitations that include specialized training and a more comprehensive treatment protocol. Such factors may limit its cost-effectiveness and accessibility for primary care, especially in rural settings that often have limited mental health care resources. Further research is necessary to explore whether abbreviated and easily administered cognitive interventions can be developed, and whether the efficacy, effectiveness, and feasibility of these interventions can be demonstrated through RCT's. Given that reviewed outcome studies also did not control for therapist contact time, it remains unclear whether improvement was due to the active treatment components of CT. In addition, larger and more heterogeneous samples will be necessary in which structured diagnostic interviews are used to assess the efficacy of CT interventions with clinical patient samples.

1.3. Cognitive–behavioral therapy

Although cognitive and cognitive–behavioral therapies have a substantial degree of overlap with regard to intervention strategies (Blackburn, 1998; Hopko, Lejuez, Ruggiero, & Eifert, 2003), the latter approaches incorporate a broader variety of treatment components that extend beyond traditional cognitive interventions (Beck et al., 1979; Ellis, 1980). For example, cognitive–behavioral protocols may be more apt to directly include problem-solving and sleep hygiene components and may provide greater emphasis on exposure or behavior activation exercises during the course of treatment. For this reason, a review of these interventions as implemented in primary care is presented as distinct

from more traditional cognitive therapy. In the context of randomized controlled trials and corresponding meta-analyses, cognitive–behavioral therapy (CBT) is considered a well-established and well-supported treatment for clinical depression (DeRubeis & Crits-Christoph, 1998), though this designation largely is based on studies conducted outside of the realm of primary care settings.

In contrast with treatment outcome studies evaluating the efficacy and effectiveness of cognitive therapy in primary care, the literature exploring the utility of CBT is somewhat more developed. An initial study by Miranda and Munoz (1994) examined CBT relative to a no-treatment control condition in patients with minor depression. Patients receiving CBT showed reduced depressive and somatization symptoms, an outcome that persisted through one-year follow-up. Other researchers also have demonstrated the benefits of CBT relative to usual care (Proudfoot et al., 2004; Schoenbaum et al., 2001; Simon, Ludman, Tutty, Operskalski & Von Korff, 2004). Interestingly, however, studies that compared CBT to supportive and non-directive counseling did not show any significant advantage of CBT for patients with both minor and major depression (Scott & Freeman, 1992; Ward et al., 2000) and some data also suggested CBT may not be superior to usual care at post-treatment (Scott & Freeman, 1992) and 12-month follow-up (Ward et al., 2000). In two of the three investigations comparing CBT with antidepressant medication, no significant differences were highlighted at post-treatment (Schoenbaum et al., 2001; Scott & Freeman, 1992). In the one study identifying medication as potentially more effective, although Miranda et al. (2003) reported that women in the medication group were less depressed than those in CBT at post-treatment (i.e., 6-months), this study had a serious methodological shortcoming in that contact time was not equated across intervention groups (i.e., for most patients CBT was provided for 8 weeks).

Considering clinicians with graduate degrees generally administer CBT in these studies, as with cognitive therapy, training requirements may limit the availability of service providers and cost-effectiveness of administering CBT in primary care. For example, in one study designed to train primary care physicians to deliver brief CBT (King et al., 2002), twenty-five PCPs attended a four-day training session. Following this training, however, primary care physicians showed no significant advantage over untrained peers with regard to depression treatment outcome. In an effort to address time efficiency and training issues, our research group recently conducted a preliminary study that assessed the efficacy of a brief behavioral activation treatment for depression (BATD; Lejuez, Hopko, & Hopko, 2002) among cancer patients in primary care (Hopko, Bell, Armento, Hunt & Lejuez, 2005). BATD differs from traditional CBT in that there is a complete focus on addressing depressive symptoms through systematically modifying environmental contingencies by increasing exposure to value-based activities (i.e., increased response–contingent positive reinforcement). No other therapeutic modalities, cognitive or otherwise, are utilized in this approach. Graduate students without prior clinical experiences administered BATD, and supporting the feasibility of the approach, treatment integrity and patient satisfaction were strong, and large effect sizes were noted on measures of depression, quality of life, and medical outcomes. Additional research has highlighted the potential for CBT to be administered in non-conventional ways (i.e. via computer or telephone) to supplement treatment provided by primary care physicians. These strategies generally have resulted in decreased depressive symptoms and increased patient satisfaction (Proudfoot et al., 2004; Simon et al., 2004; Tutty, Ludman & Simon, 2005). Although these data are preliminary, the format and success of CBT in these studies introduces the prospect of another viable treatment option for primary care.

1.4. Counseling approaches

Studies that examine counseling treatments for depression in primary care are both limited in number and somewhat equivocal. For the purpose of this review, counseling approaches included strategies such as Rogerian psychotherapy, supportive psychotherapy, or psychoeducational techniques without supplemental interventions. Accordingly, relative to other therapeutic modalities outlined in this review, these approaches are more heterogeneous and certainly not manualized in any structured fashion. Data on the efficacy of these approaches are equivocal. For example, while several studies show counseling to produce a similar or better treatment outcome than usual care and equivalence to antidepressant medication (Chilvers et al, 2001; Scott & Freeman, 1992; Ward et al., 2000), other studies demonstrate limited utility of counseling approaches over that provided by usual care (Dobscha et al., 2006; Friedli, King, Lloyd, & Horder, 1997; Simpson, Chorney, Fitzgerald, & Beecham, 2003; Swindle et al., 2003). Although these data partially suggest counseling may be a viable treatment alternative, conclusions are best perceived as preliminary due to methodological concerns. For example, several studies did not control for medication use within and between treatment conditions (Friedli et al., 1997; Simpson et al., 2003). Additionally, in contrast to several studies of PST-PC and cognitive therapy in which medical utilization was systematically monitored and controlled (Mynors-Wallis et al., 1995;

Barrett et al., 2001), the relative use of PCP services was either not defined or significantly differed between treatment and control groups (Freidli et al., 1997; Simpson et al., 2003; Ward et al., 2000). Finally, in many instances the provision of counseling services may have been too brief, with interventions also generally being non-manualized and poorly defined (e.g., Dobscha et al., 2006; Swindle et al., 2003). Consequently, given these methodological limitations, further studies are necessary to assess the potential of counseling as a stand-alone treatment in primary care. In the one study that effectively controlled for medication use, generic counseling was found to be as successful as antidepressant medication for individuals with mild to moderate depression (Chilvers et al., 2001), although patients in the medication condition showed a faster recovery rate. Additional research is necessary to elucidate the efficacy and effectiveness of general counseling strategies for individuals with more severe depression, as well as to better identify the training requirements for providers and the appropriate duration of therapy necessary to observe positive treatment gains.

1.5. Interpersonal therapy

Interpersonal psychotherapy (IPT; Klerman et al., 1984; Weissman, Markowitz, & Klerman, 2000) is a time-limited psychodynamic intervention that focuses on problems within *current* interpersonal relationships that are related to unresolved grief, role transitions, interpersonal role disputes, and interpersonal skill deficits. Although a substantial number of studies have documented the effectiveness of IPT with adolescent, adult, and geriatric samples (cf. Weissman et al., 2000) and IPT is considered a well-established and well-supported treatment for clinical depression (DeRubeis & Crits-Christoph, 1998), minimal research has examined the use of the intervention in primary care settings. The initial study by Schulberg et al. (1996) compared the relative efficacy of IPT, pharmacotherapy (i.e., nortriptyline), and physician usual care in treating major depression in the context of four academically affiliated primary care facilities. Doctoral level clinical psychologists provided IPT over a course of sixteen sessions. Relative to usual care, depressive symptoms decreased more rapidly among individuals randomized to the IPT and medication conditions. Treatment outcome also varied as a function of depression severity. Among patients who were severely depressed, the IPT and medication groups showed similar treatment response rates. Patients who were less severely depressed exhibited more rapid symptom attenuation when treated with nortriptyline relative to IPT. Consistent with AHCPR recommendations, this study supported the notion that IPT may be an effective intervention to be used as either a secondary strategy to medication (non-responders) or in conjunction with medication to treat individuals with more severe depression. A more recent study examined the combined and independent effectiveness of medication (i.e., sertraline) and IPT in the treatment of individuals with dysthymia (Browne et al., 2002). Patients receiving the combined intervention showed similar treatment response rates as compared with the medication alone condition, and both of these treatment approaches were more effective than IPT administered in isolation. In this study, lack of compelling support for IPT as a stand-alone intervention may have been due to methodological weaknesses that included the provision of relatively few sessions of IPT (mean = 10 sessions) provided within a very large pre-post–treatment time interval (i.e., 6 months). Novice therapists (1–2 years experience) and associated questions of treatment adherence (which was assessed in a very non-systematic manner) also may have been factors affecting treatment outcome.

In response to the unique challenges associated with treating clinical depression in primary care, Klerman et al. (1987) developed interpersonal counseling (IPC), a brief six-session intervention based on IPT, but designed to be administered by individuals who may not have mental health training such as nurse practitioners (see Weissman et al., 2000 for a more detailed account of how IPC was adapted). Three studies have been conducted that assess the effectiveness of this abbreviated approach. Incorporating an undiagnosed sample of individuals with elevated depressive symptoms, Klerman et al. (1987) demonstrated that IPC could feasibly be implemented by nurse practitioners and that IPC was more effective than usual care in reducing depressive symptoms. IPC was not subsequently associated with reduced mental health care utilization, however, and cost offset was not demonstrated. In a more recent study that involved a slightly longer duration of treatment (10 sessions), IPC was found to be more effective than usual care in reducing depressive symptoms in geriatric patients, a finding maintained at 6-month follow-up (Mossey, Knott, Higgins, & Talerico, 1996). Finally, Guthrie and colleagues (2004) studied the effectiveness of a 12-session psychodynamic intervention that shared similarities with IPC, including a focus on the patient–therapist relationship as a tool for resolving interpersonal issues, the perspective that interpersonal problems are the primary etiological factor in depression, and a focus on understanding and modifying patient's social roles and behaviors in the larger social context. The intervention differs from IPC in that more intense focus (with psychodynamic therapy) is placed on patient–therapist social behaviors in interpreting client's problems, and less emphasis is placed on assessing

and treating role transitions, implementing skills training, and engaging in inter-session practice exercises. Although it was demonstrated that this intervention might effectively reduce depressive symptoms, this study was characterized by significant methodological shortcomings that included no control group and a small sample size (Guthrie et al., 2004).

IPT is by all indications an empirically valid treatment for depression as measured in the context of a number of randomized controlled trials (DeRubeis & Crits-Christoph, 1998). It also is evident that this intervention is understudied in the realm of primary care, with one of the two defining studies of IPT supporting comparable efficacy with pharmacotherapy, and two studies supporting the abbreviated IPC as superior to usual care in treating depression. Although the treatment duration and expertise required of traditional IPT may limit its feasibility in primary care, IPC may be a reasonable alternative. Considering the paucity of data exploring the effectiveness of this abbreviated method, further programmatic research is necessary that incorporates samples of well-diagnosed depressed patients, comparison conditions that involve empirically-supported pharmacological and psychosocial interventions, longer-term follow-up assessments, and evaluation of factors predictive of treatment response.

1.6. Pharmacotherapy trials

Due to factors that include unavailability of psychotherapy resources, effective marketing of antidepressants (Antonuccio, 1995), and the cost-effectiveness and affordability (if insured) associated with treatment via antidepressant medications, pharmacotherapy is the most commonly used intervention for depression in primary care (Robinson, Geske, Prest, & Barnacle, 2005; Schulberg et al., 1997). Pharmacotherapy generally involves medications that fall into one of the primary antidepressant drug classes [i.e., tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs), norepinephrine reuptake inhibitors (NRIs), atypical antidepressants (e.g., bupropion and mirtazapine), and monoamine oxidase inhibitors (MAOIs)]. Selecting the most appropriate medication involves attention to treatment history, co-existent psychiatric and medical problems, likelihood of side effects, safety in overdose, and expense (Depression Guideline Panel, 1993; Simon, 2002; Thase & Kupfer, 1996).

In the general literature, a meta-analysis was conducted to examine 150 randomized trials that compared the efficacy of antidepressants (Mulrow et al., 1998). Newer pharmacological interventions (i.e., SSRIs, SNRIs) were reported to be no more effective than older medications (i.e., TCAs, MAOIs), and no difference was evident in discontinuation rates as a function of medication type. Within the context of primary care and presented in Appendix Table 1, a recent meta-analysis of 10 studies compared the efficacy of both TCA and SSRI antidepressants to placebo treatment (Arroll et al., 2005). This review showed patients receiving antidepressant medication in primary care to have superior outcomes to those receiving placebo and indicated that both medication classes were effective in this setting. This same research group conducted a meta-analysis of 11 randomized trials comparing SSRIs and TCAs (MacGillivray et al., 2003) and found no significant differences in treatment efficacy, although an effect of treatment compliance was observed in that patients receiving TCAs were more likely to withdraw from treatment due to adverse side effects. Among the studies included in this review, Ravindran et al. (1997) demonstrated similar efficacy of clomipramine and paroxetine for reducing depression and anxiety, but highlighted that patients receiving paroxetine showed greater tolerability of the medication. It also is apparent that relative to patients prescribed a TCA, those taking an SSRI may not only be more likely to complete treatment, but also may demonstrate a quicker response to treatment (Freed, Goldney, Lambert, Tiller, & Johnston, 1999). Comparing medications within the SSRI drug class, Kroenke et al. (2001) demonstrated that patients on each of three SSRI medications (paroxetine, fluoxetine, and sertraline) had similar improvements in medical, social and mental health outcomes, as well as similar rates of adverse side effects and treatment discontinuation. Several studies not included in the MacGillivray et al. (2003) review generally support these findings. For example, across several studies, patients who were prescribed third generation antidepressants (SNRIs, NRIs) exhibited greater treatment compliance than those prescribed first generation medications such as TCAs and MAOIs (Simon et al., 1999; Montgomery, Doyle, Stern, & McBurney, 2005). Consistent with the MacGillivary et al. findings (2003), other researchers have proposed minimal differences in efficacy as a function of drug class (Anderson, 2000), although recently it was proposed that newer-generation antidepressants (SSRIs, SNRIs, atypical antidepressants) may be associated with lower suicide rates (Gibbons, Hur, Bhaumik, & Mann, 2005) and that significant methodological shortcomings may be responsible for null findings in pharmacological treatment outcome research (Thase, 2002).

Data generally support the notion that newer-generation antidepressants (particularly SSRIs) are an effective first-line option for the treatment of depression in primary care due to their superior tolerability. However, it also is evident

that practical and methodological limitations associated with pharmacological treatment outcome research merit attention in future research (cf. Thase, 2002). For example, effective management of depressive symptoms via antidepressant medications in primary care has been questionable (Coyne et al., 2002; Katon, von Korff, Lin, Bush, & Ormel, 1992), and antidepressants demonstrated as efficacious in clinical trials are not effective under conditions of routine care (Coyne & Thompson, 2003). Second, only a handful of studies conducted in the primary care environment have involved utilization of well-diagnosed depressed patients (e.g., 4 of the 11 studies cited in MacGillivray et al., 2003). As such, we are uncertain as to whether positive effects of pharmacological interventions extend beyond non-clinical (subsyndromal) samples toward clinically depressed patients, a population more difficult to treat (Keller et al., 2000; McCullough, 2000). Third, as only three of the pharmacological clinical trials described in Appendix Table 1 incorporated a placebo condition (Doogan & Langdon, 1994; Lepola, Loft & Reines, 2003), methodological questions arise regarding the general absence of no-treatment control conditions. Finally, as with the psychotherapy treatment outcome research, more extensive pre–post-treatment outcome assessment is necessary (e.g., both clinician and self-report measures of depression, medical outcomes, quality of life, anxiety and substance abuse assessment), as is an evaluation of longer-term post-treatment follow-up and documentation of factors predictive of treatment response.

2. Summary of treatment effectiveness in primary care

A general overview of treatment outcome data is provided in Table 1. To be included in this summary, studies had to include a randomized control design. Due to a substantial number of studies that did not involve collection of long-term follow-up data, Table 1 is based on pre-post treatment outcome data. Although this summary largely is based on primary (depression) outcome measures, in several instances there were concurrent improvements on measures of social and physical functioning as well as quality of life (e.g., Gatalan et al., 1991; Mossey et al., 1996; Unutzer et al., 2002), reduced treatment attrition and increased patient satisfaction (e.g., Katon et al., 2004; Mynors-Wallis et al., 1995; Proudfoot et al., 2004; Simon et al., 2004), or improvement as measured by other variables such as reductions in work absenteeism (e.g., Mynors-Wallis et al., 1997; Shoenbaum et al., 2001). As indicated in the table, it is clear that psychotherapy, pharmacotherapy, and collaborative care models generally are superior to "usual care" (or placebo) in the treatment of depression in primary care (i.e., 20 of 24 studies). Note that in the four studies yielding similar outcomes in the psychotherapy and usual care groups, three of these studies included a therapy condition that consisted of a fairly poorly described, non-manualized, and very brief counseling intervention (Dobscha et al., 2006; Friedli et al., 1997; Swindle et al., 2003). In the ten investigations (seven with a placebo/usual care condition) that directly compared the efficacy of psychotherapy relative to pharmacotherapy, similar outcomes were reported in six of the studies. In the remaining four studies, three studies demonstrated an advantage for pharmacotherapy and one supported psychotherapy as more beneficial. Among patients diagnosed with dysthymia, remission rates were significantly higher for patients treated with Paroxetine (80%) relative to those receiving problem-solving therapy (57%; Barrett et al., 2001). There also were data to suggest dysthymic patients responded better to Sertraline (60%) or Sertraline combined with interpersonal psychotherapy (58%), than those treated with interpersonal psychotherapy alone (47%; Browne et al., 2002). Finally, although there was no difference between interventions at 12-month follow-up and generic counseling was used as opposed to a validated psychotherapeutic approach, recovery rates appeared somewhat more rapid in a non-clinical sample of individuals treated with pharmacotherapy (Chilvers et al., 2001). In contrast to these findings, Shoenbaum et al. (2001) demonstrated (in a quality improvement program) that relative to a pharmacotherapy condition, depressed

Table 1
Relative efficacy of psychosocial and pharmacological interventions

	Combined care	Psychotherapy	Pharmacotherapy	Placebo/usual care	Similar outcome
Psychotherapy vs. usual care *Studies=17*		13			4
Pharmacotherapy vs. placebo *Studies=3*			3		
Psychotherapy vs. pharmacotherapy vs. placebo/usual care *Studies=7*		1	2		4*
Psychotherapy vs. pharmacotherapy *Studies=3*			1		2
Collaborative (combined) care vs. usual care *Studies=4*	4				

Note.*Comparability between psychotherapy and pharmacotherapy (both superior to placebo/usual care).

patients receiving cognitive–behavior therapy had fewer depressed days and more days of employment at post-treatment.

Although these data generally support similar efficacy for pharmacological and psychotherapeutic interventions in the treatment of individuals with mild to moderate depression (and dysthymia), a number of interpretive limitations are inherent as indicated in previous sections. In particular, a wide array of treatment providers and differential levels of expertise, different treatment durations, disparate outcome measures, inconsistent inclusion and exclusion criteria, frequent use of patients who are not well-diagnosed via structured diagnostic strategies, and limited long-term follow-up data hinder efforts to make definitive statements on the relative effectiveness of depression interventions in primary care. Moreover, feasibility concerns are apparent, as is the need to assess the effectiveness of different interventions as a function of specific patient characteristics (e.g., age, depression severity, co-existing mental and physical symptomatology).

Despite the need to address these methodological limitations in ongoing research programs, a few conclusive statements may be made about the current status of depression treatment in primary care. First, based on established guidelines for evaluating the efficacy of psychosocial interventions (Chambless & Hollon, 1998), the following conclusions may be made about the efficacy of specific treatment modalities in primary care. Both problem-solving therapy (PST-PC) and interpersonal psychotherapy would be considered efficacious interventions for major depression and possibly efficacious for minor depression or dysthymia (i.e., some equivocal findings and minimal research database). Cognitive–behavioral therapy is a possibly efficacious treatment for both major depression and minor depression or dysthymia (i.e., some empirical support), though more programmatic research is necessary to address methodological limitations that include use of differential self-report and behavioral outcomes (e.g., Schoenbaum et al., 2001), and the substantial differences in mode of administration (i.e., face-to-face contact, telephone intervention, computer-administered therapy). Cognitive therapy is less supported, but would be considered a possibly efficacious intervention for depression given encouraging findings mixed with the weak effect sizes and loss of treatment gains (at follow-up) characterizing the two randomized controlled trials (Scott et al., 1997; Teasdale et al., 1984). Cognitive therapy has not been investigated among patients with either minor depression or dysthymia. Counseling approaches generally would not be considered efficacious treatments due to equivocal outcome data, lengthy or ill-defined treatment intervals (Chilvers et al., 2001; Simpson et al., 2003) and inadequately described treatment protocols. Finally, by most standards, pharmacotherapy is considered an efficacious approach for treating both major depression and dysthymia (APA, 2000).

As a second important conclusion, psychotherapy generally appears to be as effective as pharmacotherapy, and there are some data to suggest patient relapse may be attenuated following treatment with psychotherapy (Munoz et al., 1994; Paykel et al., 1999). Third, the predominating psychosocial intervention represented in the primary care literature is PST-PC. The effectiveness of PST-PC interventions is supported through data presented in nine outcome studies, and the feasibility of PST is evident in studies that demonstrate the ease with which health care professionals can be trained to effectively deliver the intervention. Fourth, it seems clear that interventions such as cognitive–behavioral therapy and interpersonal psychotherapy show promise in the realm of primary care, although these interventions are relatively less studied, particularly interpersonal psychotherapy. Fifth, due to time restrictions, reimbursement considerations, and availability of trained mental health professionals in primary care, logistical limitations may preclude use of certain psychosocial interventions in primary care. For example, utilization of cognitive therapy, considered an efficacious intervention (DeRubis & Crits-Christoph, 1998), may be limited in primary care by the length of treatment and expertise required to deliver the therapy. Sixth, pharmacotherapy is the first-line intervention for depressed primary care patients. As illustrated, however, effective management of depressive symptoms via antidepressant medications is questionable (Coyne & Thompson, 2003; Coyne et al., 2002; Katon et al., 1992). Potentially due to limited training, expertise, and continuing education requirements of primary care physicians, they may be less likely to prescribe newer medications and may frequently provide an inadequate dosage and duration of treatment to patients (Lawrenson, Tyrer, Newson, & Farmer, 2000; Simon et al., 1993). Finally, many depressed primary care patients are dissatisfied with the treatment they receive (Wells et al., 1999), and it is evident that if given the option, many patients demonstrate a preference for psychotherapy over pharmacotherapy (Chilvers et al., 2001; Priest et al., 1996; Zeiss & Thompson, 2003).

Initial recommendations from the Agency for Health Care Policy (AHCPR, 1993) generally favored pharmacotherapy as a first-line treatment for patients with (mild-moderate) depression in primary care due to a "substantially greater body of research supporting the use of pharmacological interventions." The revised guidelines (APA, 2000) allowed more flexibility insofar as implementing psychosocial treatments for mild to moderately depressed

individuals, but generally stipulated that medications are required for more severe depressions (Hollon & Shelton, 2001). Considering the time resources, expertise, and reimbursement considerations associated with providing psychosocial interventions in primary care along with comparability with pharmacotherapy in terms of treatment efficacy, it is understandable why pharmacotherapy may be a more feasible treatment option, particularly within smaller health care systems. However, given the encouraging data on psychotherapeutic interventions in primary care, utility of psychotherapy in treating individuals with severe and chronic depression (DeRubeis et al., 2005; Keller et al., 2000; McCullough, 2000), and some concerns regarding the effective use of antidepressants, time-limited interventions such as PST-PC, IPC, and some cognitive–behavioral methods may be reasonable alternatives. These empirically-supported interventions may not only effectively treat depressive symptoms (and potentially more chronic depressions), but also might increase patient satisfaction, have more enduring and greater breadth of effects than medications (Hollon & Shelton, 2001), and also have the potential to be administered by individuals untrained in the provision of mental health services, all factors that would improve continuity of care. Indeed, since the publication of the AHCPR treatment guidelines, research focused on developing and modifying effective psychotherapeutic interventions for primary care has continued to grow and diversify. Addressing issues highlighted above, further research is therefore needed to assess the value of psychosocial interventions for depressed primary care patients and determine whether further reexamination of AHCPR policies is warranted.

3. Predictors of treatment response and recovery

In spite of the broad selection of psychosocial and pharmacological interventions for depression, a significant proportion of individuals do not respond to treatment or relapse rapidly following termination of treatment. Approximately 33–50% of depressed patients may be resistant to pharmacotherapy (Fava & Davidson, 1996), with similar treatment response rates for primary care patients treated with psychotherapy (e.g., Barrett et al., 2001; Simpson et al., 2003). Non-responsiveness to treatment and early relapse are substantial problems in that these factors are linked with higher service use and poorer health outcomes in primary care (Simon et al., 2002). Identifying factors that contribute to treatment response and recovery as well as those associated with relapse is therefore critical toward improving depression care.

In the more general literature extending toward academic clinical trials and psychiatric samples, a number of common variables are associated with reduced treatment response and early relapse. These factors include limited confidence in the intervention, poor therapeutic alliance, treatment non-compliance and failure to complete homework exercises (psychotherapy), increased severity and chronicity of depression, family history of depression, presence of a personality disorder (but see Mulder, Joyce, & Luty, 2003), co-existent Axis I disorders, perceived social stigma, increased cognitive and/or social dysfunction, marital problems, and double depression (Addis & Jacobson, 1996; Arnow et al., 2003; Duggan et al., 1998; Jarrett, 1995; Kung & Elkin, 2000; Mynors-Wallis & Gath, 1997; Sirey et al., 2001; Sotsky, Glass, Shea, & Pilkonis, 1991). Given the emphasis on psychiatric samples, it is interesting to speculate on whether variables linked to limited treatment response and relapse in primary care patients differ from those of psychiatric patients, partially because the former group generally has fewer co-existent psychiatric problems, less severe depression at treatment outset, and thus potentially a better prognosis (Schulberg et al, 1995; Simon & Von Korff, 1995).

Although the topic is relatively understudied in primary care samples, the answer to this question appears to be that similar predictors of outcome exist across psychiatric and primary care samples. In particular, primary care patient characteristics linked to poor treatment response include increased depression severity at pre-treatment, lower levels of education, unemployment, older age and male gender, non-adherence to treatment, presence of personality disorders and co-existent Axis I disorders, and decreased social functioning (Casey et al., 2004; Frank et al., 2002; Hegel et al., 2002, 2005; Katon et al., 2002; Roy-Byrne, Russo, Cowly, & Katon, 2003; Sherbourne, Schoenbaum, Wells, & Croghan, 2004). Individuals who present with suicidal ideation and increased neuroticism also are at a greater risk for poor treatment response and early relapse (Katon et al., 2002). Interestingly, one study demonstrated that the number of co-existent medical illnesses did not impact treatment response among older adults treated with problem-solving therapy (Harpole et al., 2005). This result is inconsistent, however, with more severe medical problems and increased pain severity both being highlighted as negatively affecting the efficacy of psychosocial and pharmacological interventions (Bair et al., 2004; Katon et al., 2002). Treatment providers also have been shown to contribute to the success or failure of depression treatment through the quality of treatment provided as well as therapeutic alliance

(Frankel, 1995). For example, Hegel and colleagues (2002) showed that the expertise of therapists providing PST-PC to patients with minor depression or dysthymia was a significant predictor of patient response to treatment. Researchers also have shown robust positive relationships between physician empathy, patient satisfaction, and treatment adherence (Frankel, 1995; Van Os et al., 2004). In line with patient satisfaction, patient involvement with and preference for treatment has also been shown to play an important role in outcome (Clever et al., 2006; Lin, Campbell, Chaney, Liu, et al., 2005). For example, Lin et al. (2005) examined the difference between two groups of individuals receiving pharmacological and psychosocial treatment for depression, one matched according to their preference and the other randomized to treatment, and showed that patients who were matched to their preference demonstrated more rapid reduction of symptoms. Also consistent with data on psychiatric samples and related to longer-term recovery, Lin et al. (1998) reported that an increased number of (past) depressive episodes of major depression (i.e., chronicity) was a strong predictor of depressive symptoms at seven months post-treatment. Higher long-term recovery rates also were associated with lower baseline depressive symptoms, as well being younger, female, and of European descent (Frank et al., 2002; Schulberg, Katon et al., 1998; Schulberg, Pilkonis et al., 1998).

More specific to the realm of pharmacotherapy, adherence to antidepressant medication can be utilized as a marker of treatment response and recovery. Research suggests that the two predominant reasons for discontinuing medication are failure to achieve symptom reduction and the presence of adverse side effects (Simon et al., 1993; Maddox, Levi, Thompson, 1994). Yet another factor that may be associated with treatment outcome involves the context of treatment. Indeed, the literature suggests that patients treated by primary care physicians are more likely to discontinue medication relative to those treated within psychiatric settings (Demyttenaere, 2003; Demyttenaere et al., 2001). The discrepancy in medication adherence across settings may be partially attributable to the finding that psychiatrists may be more likely to prescribe newer antidepressants that generally have fewer aversive side effects (Simon et al., 1993).

Collectively, these data underscore the importance of developing positive patient–physician relationships, effectively ascertaining information on previous treatment history and compliance related issues, improving assessment strategies to more readily detect psychiatric problems (as well as medical diagnoses), encouraging continuing education on pharmacological interventions for depression, and problem solving around how to work with patients who are at high risk of being non-responsive to treatment or relapsing soon after treatment. Potential strategies might include the use of motivational interviewing strategies (Miller & Rollnick, 2002), the use of multimodal intervention strategies (e.g., combined psychosocial/pharmacological intervention, pain management), careful assessment of patient treatment preferences, and enhanced follow-up through collaborative care programs.

4. Treatment providers in primary care

4.1. PCP treatment

Primary care physicians (PCP's) play an integral role in the diagnosis and treatment of depression, although it has been documented that quality of care provided by PCP's is often sub-optimal (Katon et al., 1992; Lawrenson et al., 2000; Simon et al., 1993). The contention has been that many physicians may have limited knowledge about the phenomenology of clinical depression and others may lack the time and communication skills necessary to ascertain whether someone is depressed (Badger et al., 1994; Williams et al., 1999). For example, physician awareness of DSM-IV (American Psychiatric Association, 1994) diagnostic nomenclature generally is limited (Williams et al., 1999), and the ability of PCP's to provide depressed patients with empathy and coping strategies may be inferior to that provided by traditional mental health care providers (Roter et al., 1997; Van Os et al., 2004). With respect to contextual limitations imposed on PCP's, the average primary care appointment is approximately thirteen minutes (Williams et al., 1999), a factor that undoubtedly limits the ability of physicians to teach patients coping skills or discuss physical and mental health issues beyond those directly associated with presenting problem(s).

It is encouraging that some research suggests physician training may improve patient outcomes (Tiemens et al., 1999; Van Os et al., 2004). For example, Van Os and colleagues (2004) conducted a 20-hour training program designed to increase physician skill in diagnosing and treating clinical depression. Following training, physicians prescribed more antidepressants, demonstrated improvement insofar as providing adequate dosages and duration of medication, were evaluated as having increased communicative skills, and had improved patient treatment response rates. In a recent meta-analysis assessing the effectiveness of physician-delivered psychosocial interventions, Huibers, Beurskens, Bleijenberg and van Schayck (2003) concluded that although there is a paucity of data exploring the

effectiveness of psychosocial interventions administered by PCP's, there has been growing support for the ability of PCP's to effectively learn and implement PST-PC for depression (Mynors-Wallis et al., 1995, 2000). In contrast to these findings, however, other researchers have reported that physician training programs may be ineffective toward improving diagnostic and intervention skills (Gask et al., 2004; Lin, Simon, Katzelnick & Pearson, 2001), and that skills acquired as a result of physician training may diminish substantially over time (Lin et al., 1997).

In summary, research examining the effectiveness of training medical personnel to recognize and treat clinical depression is minimal, and data on the usefulness of structured training protocols to improve patient outcomes are equivocal. However, it also should be noted that a substantial proportion of studies cited in this review, particularly for PST and IPT, involved successful implementation of psychotherapy by PCP's and nurses (or nurse practitioners). The importance of continuing to explore whether these interventions and abbreviated cognitive–behavioral strategies can be effectively provided by medical personnel is critical, particularly in the context of providing continuity of care to individuals without easy access to mental health services (e.g., rural communities, individuals with limited insurance coverage). Two potential solutions to this issue may involve the utilization of collaborative care programs and the integration of mental health physician extenders in primary care settings.

4.2. Collaborative care

General principles of a collaborative care system include physician education, patient education, access to specialist care, organized methods of treatment management and follow-up, and often a physician-extender or mental health specialist (Katon et al., 1999; Oxman, Deitrich, & Schulberg, 2003). Collaborative care programs were initiated to increase treatment efficiency and effectiveness, as a partial remedy for time restrictions imposed upon PCP's, in response to patients frequently not following up with PCP referrals to psychiatric specialty care, and to facilitate better communication between PCP's and mental health professionals (Magruder & Norquist, 1999). Collaborative care models of depression have provided encouraging results in that they generally have yielded positive treatment outcome in patients with clinical depression (Katon et al., 1995, 1999, 2004; Unutzer et al., 2002). More specifically, using a collaborative care program that included medication surveillance, education, and psychiatric consultation, patients exhibited substantial pre–post-treatment outcome that was maintained at 2-months post-intervention (Katon et al., 1995, 1999). Relative to usual care, collaborative care models also have resulted in greater adherence to medication and greater treatment satisfaction (Katon et al., 1995, 2004). Equally as important in assessing treatment feasibility, collaborative care models may improve cost-effectiveness in the long-term (Katon et al., 1999). In contrast to these positive results among patients with major depression, however, collaborative care in the treatment of minor depression did not result in differential patient outcome relative to usual care and was not justified as a cost-effective method of intervention (Von Korff et al., 1998).

4.3. Mental health specialist/physician extenders

Consistent with the philosophy of collaborative care models and to bridge the gap between physician and specialty care, several treatment programs have utilized depression care managers (DCM) (Oishi et al., 2003; Oxman, Deitrich, & Schulberg, 2003). The position typically is filled by a variety of medical professionals (i.e. nurses, masters level therapists, or psychologists) and the responsibility of the position can vary depending on the nature of the health care system (Unutzer et al., 2002; Oxman et al., 2003). For example, the DCM can meet weekly with psychiatrists to discuss patient progress and ongoing treatment goals, serve as a liaison between a PCP and psychiatrist, monitor patient follow-up in a more structured fashion to enhance treatment adherence and identify problems that are often not addressed in the brevity of physician visits, or may provide psychotherapy in the primary care setting as an alternative or adjunct to medication. Incorporation of a DCM has been shown to be time efficient for psychiatrists and allows for more patients to benefit from specialist expertise (Oxman et al., 2003). DCMs also have been useful toward improving the quality of depression care as demonstrated by decreased depression severity, increased patient satisfaction, less functional impairment, and greater quality of life (Katon et al., 2004; Mynors-Wallis et al., 1997, 2000; Mossey et al., 1996; Oxman et al., 2003; Unutzer et al., 2002; Williams et al., 2000).

Although the prospect of incorporating DCMs into primary care is promising, rather substantial obstacles require attention, particularly the logistical issues and training requirements associated with the position within typical health care environments. For example, studies utilizing DCMs generally have budgeted for all aspects of training

and financial support for the position (Oxman et al., 2003; Oishi et al., 2003), so it may be particularly difficult for smaller health care systems to financially support a full-time depression specialist. Within healthcare systems, a limited number of individuals presumably would serve as a DCM, thereby also limiting training opportunities as well as guidance and support with tasks associated with the position. Due to such factors, following the termination of research studies incorporating a DCM, the position typically is discontinued (Katon et al., 2004; Oishi et al., 2003). One group of researchers recently was able to overcome these obstacles by utilizing resources inside of the existing health care network and by limiting the duties of the DCM (Dietrich et al., 2004). In this QI program, the DCM served in the role of liaison between the patient and psychiatrist through phone conferencing, and contacted patients on a regimented schedule to follow-up on their treatment needs. Since the DCM's duties were limited, the training requirement entailed only 4–8 hours of instruction. This intervention showed a striking improvement in patient response to treatment, sustained remission rates, and satisfaction with treatment compared to the control group, and thus may represent a viable model to replicate in today's health care system.

5. Cost-effectiveness

Evaluating the cost-effectiveness of depression interventions is a critical topic to address in primary care due to the steadily rising costs of medical and mental health services, an imbalance between mental health needs and the availability of mental health resources, and a determined movement toward utilizing affordable, empirically-supported treatments within primary care (Barrett, Byford, & Knapp, 2005; Lave, Frank, Schulberg & Kamlet, 1998; WHO, 2004). Economic issues surrounding depression interventions also are complicated by the fact that depressed primary care patients often have co-existent (and frequently severe) medical problems, increased use of medical health services, and poorly managed depression (Katon & Ciechanowski, 2002; Simon & Katzelnick, 1997; Simon, Ormel, VonKorff, & Barlow, 1995). Indeed, depression poses a substantial financial burden on society due to the direct (health care, medication) and indirect (lost wages, absenteeism) economic costs of treating depression, with 400–500 million dollars spent annually in direct costs (Jonsson & Rosenbaum, 1993; Montgomery et al., 2005). For these reasons, researchers have begun to develop methods to quantify the associated costs and benefits of specific depression interventions, strategies that generally assess the fixed costs of treatment relative to outcome. Across studies, measurement of treatment outcome typically incorporates some combination of the following variables: depressive symptomatology, quality of life, medical resource utilization, disease-free days, and worker productivity (cf. Barrett et al., 2005).

As indicated in Table 2, cost analysis techniques have been utilized to assess specific forms of psychotherapy in relation to usual care, with data yielding inconsistent findings. Some investigators have indicated that counseling strategies and cognitive–behavioral therapy may result in improved outcomes when supplementing usual care strategies, but also are associated with significantly greater costs (Bower et al., 2003; Scott & Freeman, 1992; Scott et al., 2003). In a similar finding, Lave and colleagues (1998) demonstrated that although IPT and pharmacotherapy were clinically effective treatments, the cost of providing both treatments was substantially higher than that associated with usual care. There also are instances where costs associated with supplementing usual care with psychotherapy resemble costs associated with usual care alone. In these studies, superior outcomes are sometimes noted such as those associated with incorporating brief IPT (Guthrie et al., 1999) or couples therapy for depressed individuals (Leff et al., 2000). In other instances, however, the addition of strategies such as self-help CBT techniques and short-term counseling were cost-effective but did not result in superior outcomes (Richards et al., 2003; Simpson et al., 2003). Finally, there are a couple of studies that provide support for the cost-effectiveness of primary care (psychosocial) depression interventions. Nurse-administered problem-solving therapy (PST-PC) may be a cost-effective treatment from a societal perspective in that patients treated with PST-PC exhibited an increase in work productivity as a result of fewer absences, an outcome that offset the initial higher treatment cost associated with the psychotherapy (Mynors-Wallis et al., 1997). It also is evident that computer-administered CBT interventions may be a cost-effective alternative, with the increase in health-related service costs far below economic increases associated with fewer work absences (McCrone et al., 2004).

More comprehensive data are available from cost analyses that directly compare pharmacotherapy with psychotherapy. In a meta-analysis of 58 studies, it was concluded that there was limited evidence for the cost-effectiveness of psychosocial interventions relative to pharmacotherapy, primarily due to the higher initial costs of providing psychotherapy (Barrett et al., 2005). Narrowing the scope to the cost-effectiveness of pharmacotherapy

Table 2
Cost-effectiveness of psychosocial and pharmacological interventions in primary care

Investigation	Adjoining efficacy study	Findings
McCrone et al. (2004)	Proudfoot et al. (2004)	▪ Cost-effectiveness was assessed for computerized CBT relative to usual care. ▪ Cost-effectiveness outcome measures: service costs, lost-employment costs, improvement in BDI scores (40 lira/I-unit improvement). ▪ Using a net benefit analysis, there is an 81% chance computer therapy is cost-effective.
Bower et al. (2000)	Ward et al. (2000)	▪ Cost-effectiveness was assessed for CBT, Non-directive counseling, and usual care ▪ No significant difference was observed at 4 and 12 mo. between the three treatments on the following measures: direct costs, production losses, or societal costs.
Lave, Frank, Schulberg & Kamlet (1998)	Schulberg et al. (1996)	▪ Cost-effectiveness of Interpersonal Psychotherapy (IPT), Nortriptyline (NT), usual care. ▪ Cost-effectiveness was assessed by generating a ratio of the (direct) incremental costs to the incremental effectiveness (Disease-Free days and quality adjusted years). ▪ Patients receiving NT had slightly better outcomes and economic costs than IPT. Both treatments (NT and IPT) produced superior outcomes to usual care, but more expensive.
Mynors-Wallis, Davis, Gray, Barbour & Gath (1997)	n/a	▪ Cost-effectiveness assessed for problem solving treatment provided by community nurses relative to physicians' usual care. ▪ Problem-solving treatment resulted in fewer disability days and fewer days off of work. Although the initial treatment cost was higher for problem-solving treatment, this was offset by the reduced cost associated with fewer missed days of work.
Scott, Palmer, Paykel, Teasdale, & Hayhurst (2003)	n/a	▪ Cost-effectiveness of a relapse prevention effort was assessed using random assignment to two treatment conditions: cognitive therapy + antidepressant medication + clinical management vs. antidepressant medication + clinical management alone ▪ Cumulative relapse rates in the cognitive therapy group were significantly lower than in the control group (29% *v.* 47%). Incremental cost (the difference in mean cost divided by the difference in the proportion of patients who were relapse-free) in patients receiving cognitive therapy was significantly lower than the overall mean costs of cognitive therapy.
Bower et al. (2003)	Meta-analysis of 4 articles assessing cost-effectiveness of counseling compared to usual care in primary care.	▪ Counseling showed a significantly higher direct cost per patient as compared to usual care in the short-term. ▪ This analysis demonstrated that the statistical limitations of cost-effectiveness analyses can be overcome by pooling data.
Barrett et al. (2005)	Meta-analysis of 58 articles.	▪ Psychotherapy is not a cost-effective treatment option as compared to pharmacotherapy. ▪ Newer antidepressant medications (SSRIs) may be more cost-effective than older drugs.
Guthrie et al. (1999)	n/a	▪ Cost-effectiveness of a relapse prevention effort was assessed using either 8 weekly sessions of psychodynamic-interpersonal psychotherapy or usual care. ▪ Patients randomized to therapy had significantly reduced psychological distress and improved social functioning 6 months after the trial. ▪ Baseline treatment costs similar for both groups. Subjects who received psychotherapy showed significant reductions in the cost of health care utilization in the 6 months after treatment compared with controls. The initial higher cost of psychotherapy was recovered within 6 months through reductions in health care use.
Leff et al. (2000)	n/a	▪ Cost-effectiveness assessed for antidepressant medication and couples therapy. ▪ The retention rate was significantly higher for couples therapy (15% vs. 56.8%). Subjects' depression decreased in both groups, but couples therapy showed a significant advantage at post-treatment and two-year follow-up. ▪ No appreciable difference was observed between the two treatments when the costs of the interventions were added to the costs of services.

(continued on next page)

Table 2 (*continued*)

Investigation	Adjoining efficacy study	Findings
Simpson, Corney, Fitzgerald, & Beecham (2003)		▪ Cost analysis compared short-term counseling to usual care for depressed patients. ▪ Both groups showed significant improvement, with no differences across treatment conditions at 6 or 12 months. ▪ There were no significant differences in the mean total costs, aggregate costs of services, or any service-group costs except for primary care, between the two groups.
Kendrick et al. (2006)	Kendrick et al. (2006)	▪ Cost analysis compared pharmacological treatment with fluoxetine and imipramine for depressed patients. ▪ Patients with MDD or dysthymic disorder treated with imipramine had lower treatment costs. Patients with depressive disorder NOS, showed no difference in treatment cost across the two treatment groups.
Bower & Rowland (2006)	Meta-analysis of 8 trials that assess the cost-effectiveness of counseling.	▪ High satisfaction with the use of counseling among patients. ▪ Some evidence to suggest that the overall cost of counseling and usual care are similar.
Serrano-Blanco et al. (2006)	Serrano-Blanco et al. (2006)	▪ No significant difference in cost-effectiveness between SSRI and TCA treatment groups. ▪ Cost-effectiveness acceptability curves indicated that treatment with SSRI medication was most cost-effective.

treatment, this meta-analysis also suggested that SSRI medications may be more cost-effective than older antidepressants, potentially due to greater clinical efficacy and the incidence of fewer side effects (Barrett et al., 2005). This is consistent with a meta-analysis of 62 double-blind randomized trials which suggested that although TCA medications could be prescribed at a lower cost per patient, the SSRI medications were more cost-effective when considered in terms of treatment success (Anderson & Tomenson, 1995). Also in relation to pharmacotherapy, cost analysis techniques have been used to evaluate the cost-benefit ratio of collaborative care and quality of care improvement programs (Pyne et al., 2003; Schoenbaum et al., 2001; Simon et al., 2001, 2002; Wells et al., 2000). Work within this realm generally has confirmed that improvement in depression outcome through enhanced and more structured (pharmacologically-based) treatment programs can be instituted without substantial increases in health care costs.

In summary, it is difficult to make precise statements regarding the cost-effectiveness of specific depression interventions in primary care. There is substantial variability in the cost of psychotherapy and primary care physician services across health care systems, and the assessment of costs must be evaluated within the context of the available resources. For example, the fixed cost of psychotherapy depends directly upon the training and availability of therapists. In a large health care network, it may be advantageous to employ a full-time depression care specialist who is capable of providing cost-effective therapy. Smaller networks may not have this flexibility, and therefore, may need to rely upon a more specialized treatment services. In addition to this concern, definitive conclusions are made difficult by the broad scope of outcome measures used across studies, variation in the range of costs included in economic evaluations, the absence of a standard treatment for depression or accepted form of "usual care," and inadequate study power that limits the ability to demonstrate cost differences (Barrett et al., 2005; Bower et al., 2003). In spite of these limitations, several broad conclusions can be derived. First, pharmacotherapy presently appears to be the preferred cost-effective treatment option in primary care, primarily due to substantially lower outpatient service use associated with treatment and the consistent support for its clinical effectiveness (Barrett et al., 2005). Second, there are some data to support the contention that psychosocial interventions in primary care may be cost-effective within the context of certain types of health care systems (Bower et al., 2000, 2003) and when certain treatment providers and strategies are used (Guthrie et al., 1999; Leff et al., 2000; McCrone et al., 2004; Mynors-Wallis et al., 1997). Third, collaborative care programs may be particularly useful in facilitating cost-effective interventions for depression and may be a context whereby brief psychosocial interventions may be implemented (Sturm & Wells, 1995). Finally, given the substantial impact of patient treatment preference in relation to intervention compliance and positive outcome, together with consistent findings that primary care patients often prefer psychotherapy over pharmacotherapy (Chilvers et al., 2001; Dwight-Johnson,

Sherbourne, Liao, & Wells, 2000; Unutzer et al., 2002; van Schaik et al., 2004; Priest et al., 1996), concentrated efforts must be made to further develop and assess the cost-effectiveness of brief psychosocial interventions for primary care.

6. General summary

Consistent with data obtained in the context of academic clinical trials, psychosocial and pharmacological interventions in primary care have comparable efficacy in reducing symptoms of mild-moderate depression, and predictors of treatment outcome are relatively similar across settings. Pharmacotherapy has been the most frequently used intervention in primary care and has been strongly advocated by the Agency for Health Care Policy and Research and other organizations (AHCPR, 1993; APA, 2000; Fochtmann & Gelenberg, 2005). Psychosocial treatments may represent an important alternative, however, particularly given relatively similar treatment response rates and increased patient satisfaction when these interventions are received. Although it is true that feasibility issues such as time duration, training requirements, and cost-effectiveness may limit the use of certain psychological treatments, there is growing support for the efficacy of time-limited problem-solving, interpersonal, and cognitive–behavioral therapies and preliminary evidence that alternative (computer and telephone-based) interventions may be useful as adjunctive treatments. Importantly, individuals without advanced mental health training (e.g., physicians, nurses) generally seem able to effectively provide some of these interventions (PST-PC, IPC) and there are some data (albeit equivocal) that support psychosocial treatment provision in a cost-effective manner. Nonetheless, sustained efforts are necessary to develop and assess interventions and their economic correlates. Collaborative care models and the use of depression health specialists are a particularly promising mechanism by which to improve the quality and continuity of care. As the study of collaborative care models is in its infancy, however, further programmatic research must establish the practicality of incorporating these programs within contemporary health care systems. Other limitations also are inherent in the primary care literature. For example, relative to academic clinical trials that include patient samples recruited outside the domain of primary care, the absolute frequency of primary care studies are few in number. This limited database translates into a number of important variables being relatively understudied in primary care, including potentially important differences in treatment response as a function of ethnicity, medical problems, impact of co-existent psychiatric problems, treatment adherence, and other patient characteristics. In closing, given the potential value of psychosocial interventions in primary care, it remains the responsibility of individuals in the mental health profession to continue scientific study of issues highlighted in this document as well as to advocate for increased patient access to primary care mental health services. In continuing this mission, the mental health field may be in a better position to illustrate the significance and potential contributions of psychosocial interventions and thereby further challenge current guidelines for depression management in primary care.

Appendix A

Appendix Table 1
Efficacy of psychosocial and pharmacological interventions

Study	Sample	Interventions and research design	Duration	Primary results
Problem solving treatment				
Mynors-Wallis, Gath, Day & Baker (2000)	151 PC patients ▪ Major depression ▪ HRSD ≥ 13 ▪ 18–65 years of age	Individual 1. PST-PCP 2. PST-nurse 3. SSRI Design = RCT	12 weeks (6 sessions)	▪ Improvements in all groups ▪ No significant difference between treatments ▪ No difference in outcome between treatments administered by physician or nurse
Mynors-Wallis, Davies, Gray,	70 PC patients	Individual	(0–5 sessions)	▪ No significant difference in outcome between groups (CIS, CHQ, social adjustment scale).

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Appendix Table 1 (*continued*)

Study	Sample	Interventions and research design	Duration	Primary results
Barbour, & Gath (1997)	• With emotional disorder • 18–65 years of age	1. PST-PC (nurse) 2. Usual care–PCP Design = RCT		▪ Patients receiving PST had fewer days of disability and fewer missed days of work.
Mynors-Wallis, Gath, Lloyd-Thomas, & Tomlinson (1995)	91 PC patients ▪ Major depression ▪ HRSD ≥ 13 ▪ 18–65 years of age	Individual 1. PST-psychiatrists and GP 2. Amitryptyline (psychiatrist & GP) 3. Placebo Design = RCT	12 weeks (6 sessions)	▪ Difference between PST and placebo significant. ▪ Difference between medication and PST not significant. ▪ Recovery (HRSD): PST (60%), medication (52%) placebo (27%) ▪ PST-PC lower attrition (7%) medication (19%)
Gatalan et al. (1991)	113 PC patients • Emotional disorders • PSE > 11 ▪ 18–65 years of age	Individual 1. PST-psychiatrist 2. Usual care–PCP Design = RCT	6 weeks (4 sessions)	▪ Improvement in both groups ▪ PST-PC patients had a greater reduction in emotional and physical symptom ratings. ▪ Difference maintained at 28-week follow-up.
Hegel et al. (2002)	179 PC patients • Minor depression/ dysthymia • HRSD ≥ 10 • PRIME-MD	Individual 1. PST-PC — psychologist or master-level therapist. Design = OT	11 weeks (6 sessions)	▪ Predictors of optimal response to PST-PC: ▪ Patient ability to understand treatment rationale ▪ Lower severity of depression at baseline ▪ CBT therapist providing treatment
Barrett et al. (2001)	241 PC patients ▪ Minor depression/ dysthymia ▪ HRSD ≥ 10 ▪ PRIME-MD ▪ 18–59 years of age	Individual 1. PST-PC (psychologist) 2. Paroxetine (10–40 mg/day) 3. Placebo Design = RCT	11 weeks (6 sessions)	▪ All treatment conditions showed significant improvement over the 11-wk period (HRSD). ▪ Dysthymia remission rate: PST (57%), medication (80%) placebo (44%) ▪ Minor depression remission rate: similar across groups.
Williams et al. (2000)	415 PC patients ▪ Minor depression/ dysthymia • HRSD ≥ 10 ▪ PRIME-MD ▪ Mean age = 71 years	Individual 1. PST-PC (Psychologist) 2. Paroxetine (10–40 mg/day) 3. Placebo Design = RCT	11 weeks (6 sessions)	▪ Medication and placebo were administered with clinical management and support over 6 sessions. Improvement in all groups ▪ Paroxetine more effective than placebo ▪ PST-PC not more effective than placebo
Katon et al. (2004)	329 PC patients • With diabetes mellitus and major depression/dysthymia • PHQ-9 > 10 • Mean age = 58 years	Individual 1. Collaborative care ▪ PST-DCM (nurse)▪ Medication — DCM management 2. Usual care — PCP Design = RCT	12 weeks + (PST — 6 sessions)	▪ Stepped care protocol, 2 empirically validated treatments, and DCM coordinated care. ▪ Of the intervention patients, 51.3% received medication + PST, 7.9% received PST alone, 32.3% received medication alone, and 8.5% received neither of the treatments. ▪ Intervention patients showed greater compliance to medication, less depression severity, greater treatment satisfaction.
Dowrick et al. (2000)	452 community participants • With depressive or adjustment disorders • DSM-IV diagnosis	Individual 1. Problem solving treatment — therapist Group	6–8 weeks (6 sessions PST) (8 sessions psychoeducation)	▪ Completion rate higher for PST than for psychoeducation (63% vs. 44%) ▪ At 6 months, 17% fewer PST and 14% fewer psychoeducation patients were depressed compared to controls. ▪ At 6 months the mean difference in BDI score compared to controls was −2.63 for PST and −1.50 psychoeducation.

Appendix Table 1 (*continued*)

Study	Sample	Interventions and research design	Duration	Primary results
	18–65 years of age Design = RCT	2. Psychoeducation 3. No treatment		▪ No differences between groups at 12 mo
Unutzer et al. (2002)	1801 PC patients	Individual	Up to 12 months	▪ IMPACT intervention included access to DCM: education, care management, support of medication or PST-PC
	▪ With major depression or dysthymia	1. IMPACT- DCM		▪ At 12 months, 45% improvement in intervention patients compared to 19% in control group (>50% reduction in depressive symptoms)
	▪ SCID-IV diagnosis ▪ Over 60 years of age	2. Usual care — PCP Design = RCT		▪ Intervention patients had greater quality of life, less functional impairment, decreased depression, and more treatment satisfaction.
Cognitive therapy				
Fennell & Teasdale (1982)	5 patients	Individual	~15 weeks (20 sessions)	▪ One patient showed marked decline and two a moderate decline in BDI at post-treatment.
	▪ With major depression 29–51 years of age	1. CT (Therapist) Design = OT		▪ Patients showed further improvement at follow-up.
Teasdale, Fennell, Hibbert, & Aimes (1984)	44 PC patients	Individual	~15 weeks (20 sessions)	▪ Usual care included medication management and referrals as recommended by the PCP.
	▪ With major depression BDI>20 HRSD≥14 18–60 years of age	1. CT+usual care (psychologist) 2. Usual care — PCP Design = RCT		▪ The intervention group had significantly fewer depressive symptoms at post-treatment. ▪ At 3 months, no significant difference in outcome between the groups.
Scott, Tacchi, Jones, & Scott (1997)	48 PC patients	Individual	7 weeks (6 sessions)	▪ Usual care included medication, counseling and referrals as recommended by the PCP.
	▪ With major depression BDI>20 18–65 years of age	1. BCT+usual care (psychologist) 2. Usual care — PCP Design = RCT		▪ Patients with the additional intervention showed a general trend for greater improvement. ▪ When neuroticism was controlled for, the BCT group had a significantly greater reduction in depressive symptoms and fewer relapses.
Scott, Scott, Tacchi & Jones (1994)	7 PC patients ▪ With major depression 18–65 years of age	Individual CT+medication Design = OT		▪ 4 of 7 patients: >50% reduction in symptoms. ▪ Intervention was generally well accepted. ▪ Treatment feasible within the time constraints.
Cognitive–behavioral therapy				
Miranda & Munoz (1994)	150 PC patients ▪ With minor depression ▪ BDI>18 ▪ 18–69 years of age	Group 1. CBT (psychologist) 2. Control (no intervention) Design = RCT	8 weeks (8 sessions)	▪ Patients with minor depression treated with CBT: ▪ Greater reduction in depressive symptoms. ▪ Reduction persisted thru 1-year follow-up. ▪ Reduced somatization. No change in somatization in control group. ▪ Missed fewer appointments with PCP during the following year
Schoenbaum et al. (2001)	1356 PC patients	Individual+group	6–12 months	▪ QI programs provided enhanced educational, assessment and follow-up.
	▪ With major depression or dysthymia ▪ CIDI criteria	1. Usual care (PCP) 2. QI-medication (PCP+Nurse) 3. QI therapy — CBT (psychotherapist) Design = RCT		▪ Over 24 months QI-med and QI therapy had 25 and 47 fewer days with depression and 17.9 and 20.9 more days of employment, respectively.
Simon, Ludman, Tutty, Operskalski & Von Korff (2004)	600 PC patients	Individual	5 months (8–sessions)	▪ Telephone psychotherapy patients had lower depression scores and greater treatment satisfaction compared to usual care.
	▪ SCL & PHQ criteria ▪ Mean age=45 years old	1. Usual care+telephone CBT & care management 2. Usual care+telephone care management		▪ Telephone care management alone did not statistically reduce depression scores compared to usual care, although the program did improve patient satisfaction.

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Appendix Table 1 (*continued*)

Study	Sample	Interventions and research design	Duration	Primary results
		3. Usual care Design = RCT		
Proudfoot et al. (2004)	274 PC patients	Individual	8 weeks (8 sessions)	▪ Treatment group had access to medication and social support. No restrictions on treatment methods provided to usual care group.
	▪ With depression and/or anxiety	1. Computerized CBT (nurse)		▪ Decline in BDI scores was greater for the computerized treatment compared to usual care. ▪ Computerized therapy improved work and social adjustment.
	▪ GHQ>4 ▪ CIS-R>12	2. Usual care (PCP)		▪ Greater satisfaction with computer treatment.
	▪ 18–75 years of age	Design = RCT		
Miranda et al. (2003)	267 PC patients	1. Individual or group CBT (therapist)	6 months 8 sessions	–CBT and medication interventions superior to referral to community care (HRSD scores)
	▪ Low-income minority women	2. Paroxetine	(option of 16)	–Medication group reported lower depressive symptoms at 6-month follow-up relative to CBT group
	▪ CIDI criteria	3. Referral to community care		
	▪ Age 18+	Design = RCT		
Hopko, Bell, Armento, Hunt & Lejuez (2005)	6 PC patients	Individual	9 weeks (9 sessions)	▪ Patients showed clinically significant pre–post-treatment improvement on measures of depression, quality of life, and medical outcomes as evidenced by moderate–large effect sizes (R=0.5–2.3).
	▪ HRSD & SCID-I/P	1. BATD		▪ Treatment gains maintained at 3-months.
	▪ Cancer diagnosis	Design = OT		▪ Results revealed strong treatment integrity, good patient compliance, and excellent patient satisfaction.
	▪ Mean age=46.4 years			
Ward et al. (2000)	464 PC patients	Individual	6–12 weeks 6 sessions (option of 12)	▪ All groups improved significantly over time.
	▪ BDI>14	1. CBT (therapist)		▪ Psychological treatments more effective than usual care by PCP at 4 months with no difference between CBT and counseling.
	▪ 197 — randomly assigned to treatment	2. Non-directive counseling (therapist)		▪ No significant difference between patients who selected psychological treatment and those who were randomized.
	▪ 137 — chose their treatment	3. Usual care (PCP)		▪ No significant differences among three groups at 12 months.
	▪ 130 — randomized between 2 psychological treatments.	Design = OT		
	▪ Age 18+			
Tutty, S. Ludman, E.J., Simon, G. (2005)	600 PC patients	Randomized treatment groups	Treatment phase:	▪ Telephone CBT treatment program was well accepted by population.
	▪ Physician diagnosis of depression	1. Telephone therapy (CBT)	(8–12 sessions)	▪ 80% retention rate for phone CBT intervention.
	▪ Identified as taking antidepressant medication	2. Structured case management	Maintenance:	▪ Qualitative outcome suggests the telephone delivery of CBT may be a practical and efficient method to enhance the pharmacotherapy treatment of depression in PC patients.
		3. Usual care Design = RCT	(6–12 months)	
Scott & Freeman (1992)	121 PC patients	Individual	16 weeks	▪ Improvement in all groups over 16 weeks.
	▪ Meeting DSM-III criteria for major depression	1. Usual care (PCP)		▪ At 4 weeks, patients in the medication group had ower Hamilton scores and a higher recovery rate than patients in usual care.
	▪ 18–65 years of age	2. Medication (psychiatrist)		▪ Patients in the social work intervention showed the fastest recovery rate.
		3. CBT (clinical psychologist)		▪ At 16 weeks, social work counseling had a better outcome than usual care.
		4. Social work		▪ Difference in outcome across treatments was small.

Appendix Table 1 (*continued*)

Study	Sample	Interventions and research design	Duration	Primary results
		intervention (social worker) Design = RCT		
Counseling				
Friedli, King, Lloyd, & Horder (1997)	136 PC patients ▪ Physician referral or depression ▪ Onset of illness <6 months ▪ Age 18+	Individual 1. Rogerian psychotherapy (therapist) 2. Usual care (PCP) Design = RCT	12 weeks (1–12 sessions)	▪ All participants improved over time. ▪ No significant between group differences in outcome. ▪ Greater overall satisfaction in the treatment group at 3-and 9-month follow-up.
Chilvers et al. (2001)	323 PC patients ▪ PCP diagnosis of depression ▪ 103 patients randomized to treatment ▪ 220 patients selected treatment ▪ 18–70 years of age	Individual 1. Generic counseling (therapist) 2. Medication (PCP) Design = RCT/PP	As recommended by therapist	▪ No difference between randomized treatment groups at 12 months. ▪ Patients that selected counseling did better than those randomized to the treatment. ▪ Recovery rate was faster for patients receiving medication.
Bower, Rowland & Hardy (2006)	Meta-analysis of 7 trials comparing counseling to usual care, CBT, or antidepressant medication.	n/a Design = MA	n/a	Counseling greater clinical effectiveness compared with usual general practitioner care in the short-term but not the long-term.
Simpson, Corney, Fitzgerald & Beecham (2003)	145 PC patients ▪ BDI>14 ▪ 18–70 years of age	Individual 1. Usual care (PCP) 2. Psychodynamic counseling (BAC accredited therapists) Design = RCT	12 months (6–12 sessions)	▪ Overall reduction in BDI scores over time ▪ Fewer depressive symptoms in the treatment group compared to the control group. ▪ No significant differences between the two groups at either 6 or 12 months. ▪ Reduced PC expenses did not offset cost of counseling.
Blanchard, Waterreus, & Mann (1995)	112 PC patients ▪ Depressed based on GMSI ▪ Interview ▪ Mean age= 76	Individual 1. Counseling with social support focus (nurse). 2. Usual care (PCP) Design = RCT	Average of 10 visits over 3 months.	▪ Intervention groups had significantly fewer symptoms of depression at post-treatment and 3-month follow-up.
Hedrick et al. (2003)	374 PC patients (VA setting) Major depression or dysthymia	Individual 1. Collaborative care (CC) including telephone counseling 2. Usual care Design = RCT	3 months	▪ CC associated with greater reduction of depressive symptoms at 3-month assessment. ▪ No significant differences at 9-months. ▪ Intervention increased proportion of patients receiving CBT and medications.
Swindle, Rao, Helmy, et al. 2003	268 PC patients (VA setting) Major depression	Individual 1. PCP liaison and brief counseling (telephone or face-to-face) (clinical nurse specialist).	3 months	▪ No differences in depression symptoms or patient satisfaction with treatment at 3-month post-treatment or 12-month follow-up.

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Appendix Table 1 (*continued*)

Study	Sample	Interventions and research design	Duration	Primary results
		2. Usual care Design = RCT		
Dobscha, Corson, Hickam, et al. (2006)	375 PC Patients (VA setting) Depression as defined by PHQ-9 (>10)	Individual/group 1. Depression decision support team (education, treatment adherence, brief group educational counseling)	3 months	▪ Reduced depression in both groups at post-treatment as assessed via the SCL. ▪ No main effect of intervention.
		2. Usual care Design = RCT		▪ Increased patient satisfaction and likelihood of receiving antidepressant medication at 12-month follow-up.
Interpersonal psychotherapy				
Guthrie et al. (2004)	20 PC Counselors ▪ No previous formal psychodynamic training	1. Training to deliver PIT to patients with depression or somatization disorder (8-session treatment) Design = OT	12 weeks ▪ 1 week course ▪ 3 months: weekly supervision in small groups	▪ Assessment of audio taped sessions with patients demonstrated that counselors were able to effectively deliver treatment. ▪ Fifty percent of patients treated by counselors using PIT showed improvement (n=17).
Browne et al. (2002)	707 PC patients ▪ Dysthymic disorder ▪ 18–74 years of age	Individual 1. Sertraline (SE) 2. IPT (M.A. level therapists) 3. SE+IPT Design = RCT	6 months (mean # sessions = 10)	▪ Response rates: 60.2% SE, 46.6% IPT, and 57.5% SE+IPT. ▪ No significant difference between SE and SE+ IPT. Both more effective than IPT alone in reducing depressive symptoms.
Schulberg et al. (1996)	276 PC patients ▪ With major depression ▪ 18–64 years of age ▪ HRSD>13	Individual 1. NT (PCP) 2. IPT (psychologists) 3. Usual care (PCP) Design = RCT	5 months (16 sessions)	▪ 70% of patients receiving medication or IPT were evaluated as being recovered relative to 20% in usual care (as indexed by the HRSD).
Klerman et al. (1987)	128 PC patients ▪ Patients with mild depression as measured by the GHQ ▪ Average age= 28 years	Individual 1. IPC (nurse practitioner) 2. Usual care (PCP) Design = RCT	Maximum of 6 mean # sessions = 3.4	▪ Patients in the IPC group had significantly higher treatment response (83%) relative to patients in the control condition (63%). ▪ Patients with co-existent anxiety took longer to recover but showed similar response rates to patients with major depression alone.
Mossey, Knott, Higgins & Talerico (1996)	76 patients ▪ GDS>10 ▪ 60–91 years of age	Individual 1. IPC (psychiatric nurses) 2. Usual care (PCP) Design = RCT	10 sessions	▪ At 3 months, IPC patients showed greater improvement on measures of depression as well as physical and social functioning. ▪ At 6 months, treatment response for depression was 61% (IPC) versus 35% (UC).
Bruce et al., 2004	1888 patients ▪ Major or minor depression ▪ Older than age 60	Individual 1. IPT (DCM) 2. Usual care	Not reported	▪ Suicidal ideation significantly decreased for the intervention group at 4 and 8 months ▪ No difference was found at 12 months. ▪ Intervention patients reported significantly fewer

Appendix Table 1 (*continued*)

Study	Sample	Interventions and research design	Duration	Primary results
				depressive symptoms than the control group at all time points.
		Design = RCT/PP		
Pharmacotherapy				
Freed et al. (1999)	375 PC patients	▪ Paroxetine (20 mg, $n=184$)	9 weeks	▪ Depression reduced with both medications.
	▪ MADRS>20	▪ Amitriptyline (50–100 mg/day, $n=191$)		▪ At week 9, patients treated with Paroxetine showed greater improvement.
		Design = RCT		▪ More patients compliant with Paroxetine.
Christiansen, Behnke, Black, Ohrstrom (1996)	144 PC patients	Dosage managed by PCP:		▪ Both drugs showed equal efficacy.
	▪ HRSD>15	▪ Paroxetine		▪ Paroxetine better tolerated with more adverse side effects reported by amitriptyline group.
	▪ 18–65 years of age	▪ Amitriptyline		
		Design = RCT		
Corne & Hall (1989)	100 PC patients	Dosage managed by PCP:	6 weeks	▪ Patients in both treatment conditions improved.
	▪ HRSD criteria	▪ Fluoxetine		▪ Patients taking Dothiepin improved more rapidly over the initial 2 weeks of the trial.
	▪ 18–70 years of age	▪ Dothiepin		
		Design = RCT		
Doogan & Langdon (1994)	269 PC patients	Dosage managed by PCP:	6 weeks	▪ Patients receiving Sertraline showed a greater improvement compared to placebo.
	▪ Meeting SCID-III-R criteria for current major depression.	▪ Sertraline		▪ Patients receiving Dothiepin showed no significant improvement relative to the placebo.
	▪ Age 18+	▪ Dothiepin ▪ Placebo		▪ Sertraline and Dothiepin generally well tolerated
		Design = RCT		
Rosenberg et al. (1994)	400 PC patients	Dosage managed by PCP:	6 weeks	▪ Patients in all treatment arms showed a significant reduction in depressive symptoms, with no significant differences between groups.
	▪ HRSD criteria	▪ Citalopram		
	▪ 19–65 years of age	▪ Imipramine		
		Design = RCT		
Moon, Jago, Wood & Doogan (1994).	106 PC patients	Dosage managed by PCP:	6 weeks	▪ Both medications showed similar efficacy in reducing symptoms of depression and anxiety.
	Major depressive disorder	▪ Sertraline (50–250 mg/day)		▪ Sertraline was better tolerated than Clomipramine.
	19–69 years of age	▪ Clomipramine (50–250 mg/day)		
		Design = RCT		
Ravindran, Hunter, Bray & Morton (1997)	1002 PC patients	Dosage managed by PCP:	12 weeks	▪ Both medications showed similar efficacy in reducing symptoms of depression and anxiety.
	▪ Diagnosis of depression with symptoms of anxiety.	▪ Paroxetine (20–40 mg/day)		▪ No significant differences between the treatment groups at any time point (2, 6, and 12 weeks).
	▪ MADRS>20	▪ Clomipramine (75–150 mg/day)		
		Design = RCT		
Taragano et al. (1999)	▪ 469 PC patients	Dosage managed by PCP:	8 weeks	▪ Open trial: 70% of patients responded to treatment and 52% reached complete remission.
	▪ PCP depression diagnosis	▪ Sertraline (50–100 mg/day)		▪ 26% reported side effects (most mild).
		Design = OT		
Simon et al. (1999)	471 PC patients	Dosage managed by PCP:	24 months	▪ Lower attrition in the Fluoxetine condition.
	▪ Diagnosis of major depression.	▪ Fluoxetine		▪ No significant differences between groups in terms of depression severity or quality of life.

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Appendix Table 1 (*continued*)

Study	Sample	Interventions and research design	Duration	Primary results
	▪ 18–90 years of age	▪ Desipramine ▪ Imipramime Design = RCT		
Kroenke et al. (2001)	573 PC patients ▪ PCP depression diagnosis ▪ 37 PC clinics	Dosage managed by PCP: ▪ Paroxetine ▪ Fluoxetine ▪ Sertraline Design = RCT	9 months	▪ Response in all three conditions was comparable on all outcome measures and at all time points. ▪ Drug classes showed similar incidences of adverse effects and discontinuation rates.
Lepola, Loft & Reines (2003)	469 PC patients	Dosage managed by PCP ▪ Escitalopram (10–20 mg/day) ▪ Citalopram (20–40 mg/day) ▪ Placebo Design = RCT	8 weeks	▪ Escitalopram more efficacious than placebo. ▪ By week 8, significantly more patients had responded to treatment with Escitalopram than with Citalopram or placebo. ▪ Escitalopram and Citalopram both well tolerated with similar adverse event profiles.
Thompson, Peveler, Stephenson, & McKendrick (2000)	152 PC patients • With MDD • 18–17 years of age	▪ Fluoxetine (20 mg/day) ▪ Dothiepin (75–150 mg/day) Design = RCT	12 weeks	▪ Fluoxetine patients had greater compliance. ▪ Fluoxetine patients showed greater improvement on depression and medical functioning outcomes.
MacGillivary et al. (2003)	Meta-analysis: ▪ 11 Studies (n=2951) ▪ Aged 18–70	▪ SSRI drug class ▪ Tricyclic drug class Design = MA	6–8 weeks	▪ Comparable efficacy between medications. ▪ More patients on TCA's withdrew from treatment, primarily due to side effects.
Arroll et al. (2005)	Meta-analysis: ▪ 15 studies ▪ PC patients ▪ Studies selected according to Cochrane Collaborative Handbook	▪ SSRI/placebo (n=10) ▪ TCA/placebo (n=3) ▪ SSRI/TCA/Placebo (n=2) Design = MA	6–8 weeks	▪ 56%–60% response rate to active treatment as compared to a 42%–47% for placebo ▪ Bothe TCA's and SSRI's shown to be effective. ▪ Low-dose TCA's are effective
Wade, Despiegel & Reines (2006)	590 PC patients ▪ With MDD	Dosage managed by PCP ▪ Escitalopram (10–20 mg/day) ▪ Placebo Design = RCT	12 months	▪ No aversive effects developed after an acute period of 8-weeks. ▪ Withdrawal rate: 26% ▪ Escitalopram demonstrated to be a safe and tolerable long-term treatment, with further improvement past an 8-week initial assessment.
Kendrick et al. (2006)	327 PC patients ▪ Physician diagnosis of MDD ▪ >18 years of age ▪ Included patients with comorbid physical or mental illness	Dosage managed by PCP ▪ TCA drug class ▪ SSRI drug class ▪ Lofepramine Design = RCT	Patients followed up to 12 months	▪ No significant differences in effectiveness were observed.
Serrano-Blanco et al. (2006)	103 PC patients ▪ Physician diagnosis of MDD, dysthymic disorder, or depressive disorder NOS	Dosage managed by PCP ▪ Fluoxetine	6 months	▪ Patients showed a similar improvement in MADRS ratings across treatment groups at 6 months. ▪ Patients with MDD taking imipramine showed more improvement at 30 days than on patients on fluoxetine.

Appendix Table 1 (*continued*)

Study	Sample	Interventions and research design	Duration	Primary results
	▪ 18–65 years of age	▪ Imipramine Design = RCT		
Foster et al. (1999) Sertraline Mean age= 63 years	16 male patients (VA setting) ▪ Significantly reduced symptoms of depression from pre–post-treatment. Design = OT	Dosage managed by PCP Major depression		Average=9 weeks

Measures
BATD= Behavioral Activation Treatment for Depression (Lejuez, Hopko, & Hopko, 2002).
BDI= Beck Depression Inventory (Beck, Ward, Mendelsohn, Mock & Erbaugh, 1961).
CIDI= Composite International Diagnostic Interview (Kessler et al., 1998).
CIS= Clinical Interview Scale — Computerized version (Lewis, Pelosi, Araya & Dunn, 1992).
GDS= Geriatric Depression Scale (Yesavage et al., 1983).
GHQ= General Health Questionnaire (Golderberg & Williams, 1988).
GMSI= Geriatric Mental State Instrument (Copeland, Dewey, & Griffiths-Jones, 1986).
HRSD= Hamilton Depression Rating Scale (Hamilton, 1960).
PHQ-9= Patient Health Questionnaire 9 (Spitzer, Kronke & Williams, 1999).
PSE= Problem State Examination.
SCID-I/P= Structured Clinical Interview for DSM-IV.
SCL= Hopkins Symptom Checklist Depression Scale (Derogatis, Rickels, Uhlenhuth & Covi, 1974).
Treatment abbreviations
BCT= Brief Cognitive Therapy.
CT= Cognitive Therapy.
IPC= Interpersonal Counseling.
IPT= Interpersonal Psychotherapy.
MDD= Major Depressive Disorder.
NT= Nortriptyline.
PIT= Psychodynamic Interpersonal Therapy.
Research design abbreviations
RCT= Randomized Controlled Trial.
OT= Open Trial.
PP= Patient Preference.
MA= Meta-analysis.

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