Take 3 – Practical Practice Pointers© February 3, 2020 Edition

Mental Health Edition:
Depression in 1° Care, Treatment Resistance, Lifestyle Psychiatry

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From the Literature

1) Depression Management in Primary Care – Let's Get it Right

In 2016, the USPSTF again recommended screening for depression in all adults and adolescents (aged 12-18). Key to this recommendation was the provision that "screening should be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up." These "adequate systems" were defined as a variety of practice-level interventions such as care managers, local depression treatment protocols and facilitated referrals to ensure that screen-positive patients got evidence-based care and did not fall through the cracks.

The BMJ has published what amounts to an "evidence-informed review" on depression management in primary care, where most of depression treatment occurs in the US. It is very comprehensive and serves as a good refresher to examine our systems of care for depression. This Pointer highlights the more "system-oriented" recommendations to improve the quality of depression management in primary care:

- Clinician Education – Primary care clinicians often feel ill-prepared to manage depression, so education in screening, pharmacologic management and non-pharmacologic management of depression can help. However, education alone has not been found to be effective. Education in addition to the implementation of some of the guidelines listed below has been shown by a systematic review to reduce depression symptoms in primary care patients.
- Measurement-based Care (MBC) – This system of care relies on using screening and symptom instruments (such as the PHQ-2 and -9) on a systematic basis to correctly identify depression and ensure that it is treated to remission (e.g., a score of <5 on the PHQ-9). In addition, careful tracking and follow-up - treating depression like any other chronic disease – can be effective. If the primary care practice is not suitably equipped to treat depression, ensuring a coordinated referral for treatment is important. This MBC system is necessary, but not sufficient – using these tools consistently, but allowing for the patient's context and tailoring the treatment plan to individual needs and preferences is important.
- Practice Infrastructure – Ensure staffing and systems are in place within the practice to support MBC (care coordination, registry of patients with depression, etc.).
- Broader community connections – Primary care networks or offices should establish relationships with trusted and reliable specialist partners to facilitate referrals and provide formal and informal consultation for challenging cases.
- Payment policies – There is broad recognition that current reimbursement models in healthcare generally do not adequately support or incentivize the Collaborative Care Model. With the growth of accountable care models and the recognition of depression as an underlying comorbidity for many chronic conditions, there may be greater attention to facilitating high quality depression care.

John's Comments:
Given how prevalent depression is, and how much it underlies poor control of many chronic diseases, it is very important for us to try to get this right There are enormous barriers to the ideal collaborative care model, but a few things are in our immediate control: 1) refreshing our knowledge about effective primary care management strategies for depression (pharmacologic and otherwise), 2) systematizing our assessment of symptoms for diagnosis and tracking using a validated tool (like the PHQ-2 and -9), and 3) ensuring follow-up with our patients to see if our therapy is helping and to facilitate any needed referrals.

References:

- Siu AL et al. Screening for Depression in Adults: US Preventive Services Task Force Recommendation Statement. JAMA. 2016;315(4):380-387. Link
- Ferenchick EK et al. Depression in 1° Care: part 1—screening and diagnosis. BMJ. 2019;365. Link
- Ramanuj P et al. Depression in 1° Care: part 2—management. BMJ. 2019;365. Link

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From the Literature

2) Managing Treatment-resistant Depression in Adults

Although antidepressants are often a first-line treatment for adults with moderate to severe depression, many people do not respond adequately to medication, and are said to have treatment-resistant depression (TRD). Little evidence exists to inform the most appropriate 'next step' treatment for these people. This review aimed to assess the effectiveness of standard pharmacological treatments for adults with TRD.

The authors reviewed randomized controlled trials (RCTs) with participants aged 18 to 74 years with unipolar depression (based on accepted established criteria) who had not responded to a minimum of four weeks of antidepressant treatment at a recommended dose. Interventions were: (1) increasing the dose of antidepressant monotherapy; (2) switching to a different antidepressant monotherapy; (3) augmenting treatment with another antidepressant; (4) augmenting treatment with a non-antidepressant. All were compared with continuing antidepressant monotherapy. They excluded studies of non-standard pharmacological treatments (e.g. sex hormones, vitamins, herbal medicines and food supplements).

Ten RCTs were identified (2731 participants). Nine were conducted in outpatient settings and one in both in- and outpatients. Mean age of participants ranged from 42 - 50.2 years, and most were female. One study investigated switching to, or augmenting current antidepressant treatment with, another antidepressant (mianserin – NOTE: tetracyclic antidepressant not available in the US). Another augmented current antidepressant treatment with the antidepressant mirtazapine. Eight studies augmented current antidepressant treatment with a non-antidepressant (either an anxiolytic (buspirone) or an antipsychotic (cariprazine; olanzapine; quetiapine (3 studies); or ziprasidone (2 studies)). Only one of the included studies was not industry-sponsored.

The authors found a small body of evidence showing that augmenting current antidepressant therapy with mianserin or with an antipsychotic (cariprazine, olanzapine, quetiapine or ziprasidone) improves depressive symptoms over the short-term (8 to 12

weeks). However, this evidence is mostly of low or moderate quality due to imprecision of the estimates of effects. Improvements with antipsychotics need to be balanced against the increased likelihood of dropping out of treatment or experiencing an adverse event. Augmentation of current antidepressant therapy with a second antidepressant, mirtazapine, does not produce a clinically important benefit in reduction of depressive symptoms (high-quality evidence). The evidence regarding the effects of augmenting current antidepressant therapy with buspirone or switching current antidepressant treatment to mianserin is currently insufficient. Further trials are needed to increase the certainty of these findings and to examine long-term effects of treatment, as well as the effectiveness of other pharmacological treatment strategies.

Mark's Comments:
The decision as to how to help patients with moderate-severe depression and/or refractory depression can be quite a challenge in clinical practice and the evidence for effectiveness is not robust. The 3rd reference from Pointer #1 (and below) provides a wonderful interactive graphic for a step-wise and comprehensive approach to management. In that reference, recommendations for medication augmentation for refractory moderate-severe depression in addition to an SSRI include mirtazapine (Remeron), venlafaxine (Effexor) and duloxetine (Cymbalta). It is vital to remember that medication treatment should be continued for at least six months after resolution of symptoms (PHQ $\leq$ 5) for the first episode depression to reduce the risk of relapse. Consider continuing maintenance medication for longer (2+ years) if there has been more than one episode of depression to reduce risk of relapse. Medication should be continued at the dose required to bring about resolution

References:

- Davies P et al. Pharmacological interventions for treatment-resistant depression in adults. Cochrane Database Syst Rev. 2019 Dec 17;12:CD010557. Link
- Ramanuj P et al. Depression in 1° Care: part 2—management. BMJ. 2019;365. Link

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From the Literature

3) The Emergence of the Field of Lifestyle Psychiatry

Physical activity, nutrition, and sleep are all widely regarded as fundamental aspects of human health, for both the body and the mind. The role of physical activity in psychiatry is particularly well researched, with a number of recent meta-analyses showing that physical activity can aid in the prevention and management of multiple symptoms of mental illness. Indeed, recent international guidelines now recommend exercise as a first-line treatment for mild/moderate depression and as an adjunctive intervention for severe mental illness

The existing evidence base shows that exercise is not only beneficial in the treatment of mental illnesses but can also be helpful for those experiencing subthreshold symptoms of mental illness as a comorbidity to physical illness. Given the now substantial evidence base for exercise and mental health, the key outstanding question now becomes about motivating among individuals with mental illness to engage in sufficient exercise in order to feel these beneficial effects.

Much like physical activity, our dietary food intake is a core determinant of physical health. Now, the potential impact of nutrition on mental health is also gaining increasing recognition due to large-scale meta-analyses of randomized controlled trials (RCTs) showing that both dietary interventions and certain nutrient supplements can significantly reduce symptoms of various psychiatric disorders.

However, the relationship between healthy diet and healthy mind is unlikely to persist when examining only specific food groups—and may be better conceptualized through a "whole of diet" approach. Specifically, the overall "inflammatory potential" of the diet (see December 16, 2019 Take 3) can now be calculated through scoring an individual's relative intake of "anti-inflammatory" nutrients (such as fruits, vegetables, and whole foods) against their intake of "inflammatory" foods (typically from calorie-dense processed foods and refined carbohydrates). Owing to the link between heightened inflammatory status and various mental disorders (including depression, bipolar disorder, and schizophrenia), the inflammatory potential of the diet is one key pathway thought to underlie associations between nutrition and mental health.

Similarly, sleep disturbance also holds bidirectional associations with mental illness, occurring both as a causal factor and consequence of mental ill-health,

Mindfulness behaviors play a central role in alleviating the adverse mental health outcomes of stressful conditions. and other interventions such as yoga, breathing techniques, nature therapies, and light, heat, and art-based therapies could be considered within the broader framework of Lifestyle Psychiatry. Additionally, a "newer" aspect of our lifestyle which is currently overlooked in psychiatry is our engagement with digital technologies—particularly smartphones and connected devices. Whereas a recent major review has identified several pathways through which digital technology use can influence cognition, the role of these devices in mental healthcare is not well characterized.

Mark's Comment:
Remember that the incorporation of these can be in addition to medication and should be part of a holistic and comprehensive treatment plan for our patients. It continues to baffle me how we as a society often actively resist these very accessible, affordable, and relatively simple interventions while spending billions of dollars on pharmaceuticals whose benefit/risk ratio is often marginal at best. As with most things in life, leading by example is likely an important place to start. How each of us (as health care role models) is deliberately and intentionally trying to incorporate regular exercise, healthy nutrition, good sleep hygiene, a daily mindfulness practice, and regular meaningful connection into our own lives seems worthy of reflection … and then action. The soon to be rolled out PeerRx program will offer a wonderful platform for mutual professional support, encouragement, and accountability. More information in the coming weeks.

Reference:
Firth J, et al. Lifestyle Psychiatry. Frontiers in Psychiatry. August 2019. Link

Feel free to forward Take 3 to your colleagues. Glad to add them to the distribution list.

Mark and John

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