New, Future and Emerging Treatments in Psychiatry: Surveying the landscape (selectively)

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Learning Objective

By the end of the presentation you should be able to:

- Assess pros and cons of new treatments in order to better educate patients about when a new treatment is useful and when it is not.

Disclosures

- Associate Editor, NEJM Journal Watch for Psychiatry
- Section Editor, UpToDate
- Consultant, American Psychiatric Association Committee on Practice Guidelines; member, Systematic Review Group

Overview

- When new treatments are worth implementing compared to current treatments
- New and repurposed medications in the psychiatric pipeline
- Current and emerging forms of neuromodulatory treatments
- New psychosocial treatments for common psychiatric disorders
- Current and emerging technologies applicable to treatment
- Current and emerging systems-based treatment strategies

Pranav Shah's Panel's Shopping List

- New meds
- Ketamine
- Neuromodulation
- Gut microbiomes
- Stem cell therapy
- Cannabinoids
- Hallucinogens
- Other biological, physical approaches, neutraceuticals
- Precision-Medicine
- Psychotherapies
- Technology-based
- Systems-based

Sources for Review
Aggregate, Filter, Curate, Disseminate

- **NEJM Journal Watch for Psychiatry:** Practice Changing (83 items since 2013); On the Horizon (140 items since 2013
- **UpToDate**
  - What's New in Psychiatry (six issues, published occasionally since 2016)
- **"Gray Literature" Daily emails** (Science Daily, journal TOCs, Neuroscience News, Innovation hubs, Brain and Behavior, Medscape, ClinicalTrails.Gov, etc.)
- **Healthy doses of PubMed**

CAVEATS

- **THIS PRESENTATION IS ALREADY OUTDATED** (latest refs Sept 2018)
  - 24 hour news cycle and continuous newsfeeds…….
- **FOMO** – Fear of Missing Out (especially when patients draw your attention to something new that you hadn't yet heard about)
  - Roughly 100,000 NIH funded publications/year
- **FAKE MEDICAL NEWS**
  - Fake, spun, overpromoted industry-new releases; Sensationalized reports in trade papers
- **GULLIBLE CONSUMERS CRAVING NEW TREATMENTS (Both clinicians and patients)**

Gibbon's Law:

For every PhD, there's an equal and opposite PhD

- **PRAZOSIN FOR PTSD NIGHTMARES:**
  In this major trial (N=305 randomized) involving military veterans who had chronic PTSD, prazosin did not alleviate distressing dreams or improve sleep quality.
  - *Raskind MA et al. Trial of Prazosin for PostTraumatic Stress Disorder in Military Veterans. N Engl J Med. 2018; 378:507-517.*
- **rTMS for Treatment-Resistant Major Depression:**
  In 164 randomized veterans, no significant differences in remission of depressive symptoms between active (41%) and sham (37%) treatments.
  - *Yesavage JA et al. Effect of Repetitive Transcranial Magnetic Stimulation on Treatment-Resistant Major Depression in US Veterans: A Randomized Clinical Trial. JAMA Psychiatry. 2018;75:884-893*

When might a new treatment be practice changing?

- Randomized Controlled Trials show better outcomes
  - Number Needed to Treat (NNT) vs placebo ordinarily < 4;
  - Number Needed to Harm (NNH) is very high; adverse effects are acceptable vs desperation levels
  - NNTs vs. Current Gold Standard? Is it any better or simply "me too"?
- Faster, Cheaper, Better
  - The Five As: Accessible, Affable, Affordable, Accountable, Acceptable adverse effects
- Couldn't hurt…

Disseminating New Treatments

Governing Laws

- Technologies change rapidly
- Cultures usually change slowly (beliefs, process, funding, regulation)
- Simple takes little time (easily prescribed)→ fast-track
- Complicated, costly, involves systems → might take years
- Grant supported demonstration projects often work well….
  …… until special funding disappears

Local Factors Accounting for Treatment Dissemination?(when might we ketaminize, neuromodulate or brexanolonize?

- Opinion leaders
- Peer behavior
- Institutional directives, prompts and guidelines Public demand
- Competition
- Aggressive detailing (pharmaceutical and device manufacturer advertising, detailing and lobbying)

New Medications

- **New Classes/Mechanisms**
- **Repurposed old medications**
- **New Delivery Systems**
  - Inhalation, patches, subdermal implants, three-month injections
  - Medication Sensors
  - Gamified nudges for adherence
  - Social systems to enhance adherence

Pipeline: Phase III Trials for Treatment Resistant Depression
(Efficacy, Safety & Comparison to Standard Treatments)

- **Brexanolone**, investigational neurosteroid for severe inpatient post-partum depression, 60 hr IV infusion > placebo
- **Brexpiprazole** (Rexulti -- FDA approved as adjunct)
- **Buprenorphine** (for depression and suicidal ideation)
- **Cariprazine** (Vraylar - primarily D_3 and D_2 receptor partial agonist; high D_3 selectivity; also for bipolar depression)
- **Ketamine, esketamine**

Meltzer-Brody S et al. *Lancet.* 2018 Aug 31. pii: S0140-6736(18)31551-4. *Expert Rev Neurother*, 2017, 17:593-609; *J Affective Disorders*, 2018. 227: 219–225; F1000Research 2017, 6(F1000 Faculty Rev):397; ClinicalTrials.Gov

Pipeline: Phase II Trials for Treatment Resistant Depression
(Does the treatment work?)

- Recent positive results for **Psilocybin, Ziprasidone**
- **Rapastinel** (novel IV tetrapeptide NMDA receptor modulator, rapid acting and long-term antidepressant and cognitive enhancer, enhances synaptic plasticity)
- **Minocyclin** (broad spectrum bacteriostatic tetracycline antibiotic)
- **Tocilizumab 9** (Hoffman LaRoche) **and Sirukumap** (Janssen) (monoclonal antibodies, interleukin-6 inhibitors, also for RA)

Expert Rev Neurother, 2017, 17:593-609, *J Affective Disorders*, 2018. 227: 219–225, F1000Research 2017, 6(F1000 Faculty Rev):397; ClinicalTrials.Gov

Pipeline: Emerging-Future Trials for Depression Monotherapy or Augmentation

- **GLUTAMATERGICS**
- **MONOAMINERGICS**
- **ATYPICAL ANTIPSYCHOTICS**
- **OPIOIDERGICS and related**
- **NICOTINERGIC and related**
- **OTHERS**

OTHER includes……..

ClinicalTrials.Gov

- **Tramadol**
- **Dextromethorphan** – alone and in combination
- **GABAA receptor positive allosteric modulators**
- **3β-Methoxypregnenolone:** selective microtubule-associated protein 2 (MAP2) stimulant
- **Vomeropherine** (odorless synthetic neuroactive steroid that engages nasal chemosensory receptor)
- **Purinoceptor antagonist**

OTHER includes……..

ClinicalTrials.Gov

- **DYRK1A inhibitor/nerve growth factor stimulant** (Dual specificity tyrosine-phosphorylation-regulated kinase 1A)
- **Sestrin2 modulator and consequent mammalian target of rapamycin complex 1 (mTORC1) activator**
- **OnabotulinuntoxinA (botox) – acetylcholine release inhibitor**
- **Hypocretin (orexin) OX2 receptor antagonist**
- **Vasopressin 1B receptor antagonist**

New and Emerging Drugs for Schizophrenia

- **Encenicline** (selective partial agonist of the **α_7 nicotinic receptor;** in phase III clinical trials for cognitive impairment).
- **Memantine** augmentation (as **cognitive enhancers for negative symptoms,** several positive small clinical trials)
  - Additional interest in **memantine-galantamine combination.**

Expert Opin Pharmacother. 2016;17:921; Front Psychiatry. 2018; 4;9:91

Newly Repurposed Drugs for Schizophrenia (as adjuncts)

- **Famotidine** (histamine 2 receptor antagonist);
- **Ondansetron** (serotonin 5-HT_3receptor antagonist);
- **Sodium benzoate** (enhances NMDA function by blocking metabolism of d-amino acids as a de-amino acid oxidase inhibitor);
- **Oxytocin** (mixed results at best regarding impact on social cognition, negative symptoms);
- **Raloxifene** selective estrogen receptor modulator (SERM) (mixed results);
- **Pregnenolone** progestin/steroid hormone precursor (mixed results).

Expert Opin Pharmacother. 2016;17:921; Front Psychiatry. 2018; 4;9:91

New Medication Strategies for Alzheimer's Dx

- **Target amyloid-beta (Aβ) production, Aβ aggregation, tau pathology**
- **BACE1 inhibitors** and **azeliragon**, **a RAGE inhibitor:** results pending
- **Leviteracetam**, **benfotiamine**, **scyllo-inositol** and **MTC** (methylthioninium chloride - **"methylene blue**" – a tau aggregation inhibitor).
- **Dextromethorphan-quinidine** for agitation in Alzheimer dementia

Expert Opinion on Pharmacotherapy, 2017, 18, 2417-2429

New, Repurposed, Repackaged Medications

- **Long-acting naltrexone** vs. buprenorphine for opioid use disorder (≈)
- **Valbenazine** for tardive dyskinesia
- **LAI antipsychotics** (now to q 3 months)
- **Amantadine** for TBI associated aggression
- **Nicotine patches** for late-life depression and cognitive decline – open
- **N-Acetyl Choline (NAC)** for AUD in cannabis users (30% reduction in alcohol use> placebo)

- Hammond FM et al. *J Head Trauma Rehabil.* 2017 Sep/Oct;32(5):308-318;
- Gandelman JA et al. *J Clin Psychiatry* 79(5): epub August 29, 2018.
- Squeglia LM. *Drug Alcohol Depend.* 2018 Apr 1;185:17-22.

Where are we with Ketamine?

- **IV subanesthetic single doses can quickly reduce suicidal thinking for up to six weeks, and reduce depressive symptoms for several weeks.**
  - *Am J Psychiatry* 2018, 175:150ff; 175:327ff
- **Repeated administration may be feasible and might produce better long-term results**
  - *J Clin Psychiatry*. 2018 Jul 24;79(4). pii: 17m11731;
  - *J Clin Psychopharmacol.* 2018;38:380ff.
- **Intranasal esketamine in repeated doses may be effective but abuse potential seems considerable**
  - *JAMA Psychiatry*. 2018;75:139ff;
  - *J Psychopharmacol*. 2018; 32:397ff;
  - *Ann Emerg Med*. 2017;70:203ff.

BUT……

- **Might ketamine help you feel better because it actually works as an opiate? Could ketamine be a gateway drug to opiate addiction in some patients?**
  - Williams NR et al. Attenuation of Antidepressant Effects of Ketamine by Opioid Receptor Antagonism. *Am J Psychiatry*; e-published August 29, 2018;
  - George MS. Is There Really Nothing New Under the Sun? Is Low-Dose Ketamine a Fast-Acting Antidepressant Simply Because It Is An Opioid? *Am J Psychiatry*; e-published August 29, 2018
- **Significant abuse potential merits caution, suggesting needs for regulatory controls, perhaps similar to those for buprenorphine**
  - Freedman R, et al. Can a Framework Be Established for the Safe Use of Ketamine? *Am J Psychiatry*. 2018; 175:587-589;
  - Kolar D. Addictive potential of novel treatments for refractory depression and anxiety. *Neuropsychiatr Dis Treat*. 2018;14:1513-1519.

Neuromodulation

(Three FDA approved for treatment-resistant depression)

- **ECT**
  - Hermida AP, et al. Electroconvulsive Therapy in Depression: Current Practice and Future Direction. *Psychiatr Clin North Am.* 2018; 41(3):341-353
- **rTMS** (high frequency vs low frequency?? Deep TMS?)
  - Garnaat SL et al. *Updates on Transcranial Magnetic Stimulation Therapy for Major Depressive Disorder. Psychiatr Clin North Am*. 2018; 41(3):419-431.
- **Vagus nerve stimulation**
  - Conway CR et al. Chronic Vagus Nerve Stimulation Significantly Improves Quality of Life in Treatment-Resistant Major Depression. *J Clin Psychiatry.* 2018 Aug 21;79(5). pii: 18m12178.
  - McGirr A, Berlim MT. Clinical Usefulness of Therapeutic Neuromodulation for Major Depression: A Systematic Meta-Review of Recent Meta-Analyses. *Psychiatr Clin North Am*. 2018; 41(3):485-503.

Neuromodulation: investigational

- **Transcranial Direct Current Stimulation (tDCS) / Transcranial Alternating Current Stimulation (tACS)**
  - Moffa AH et al. Transcranial Direct Current Stimulation in Psychiatric Disorders: A Comprehensive Review. *Psychiatr Clin North Am. 2018;* 41(3):447-463.
- **Auricular nerve stimulation**
  - Kong J et al. Treating Depression with Transcutaneous Auricular Vagus Nerve Stimulation: State of the Art and Future Perspectives. *Front Psychiatry.* 2018;9:20
- **Deep Brain Stimulation**
  - Lewis PM et al. Brain Neuromodulation Techniques: A Review. Neuroscientist. 2016; 22:406-21.
- **Temporal Interference Stimulation** (deep brain non-invasive electrical)
  - Grossman N. *Modulation without surgical intervention*. Science. 2018; 361(6401):461-462.
- **Low-intensity Ultrasound Neuromodulation** ("sonication")
  - Bowardy P, Greenberg BD. *Noninvasive Focused Ultrasound for Neuromodulation: A Review. Psychiatr Clin North Am.* 2018; 41:505-514

Brain Connectivity Biotyping and Targeted Intervention

- Brain connectivity patterns differ with clinical subtypes and with treatment responsivity patterns.
- These circuits provide new refined targets for neuromodulatory interventions.

- Drysdale AT at al. ***Resting-state connectivity biomarkers define neurophysiological subtypes of depression***. Nat Med. 2017; 23:28-38.
- Fischer AS et al. ***The Clinical Applicability of Functional Connectivity in Depression: Pathways Toward More Targeted Intervention.*** Biol Psychiatry Cogn Neurosci Neuroimaging. 2016; 1:262-270.

Gut Microbiome

- **Microbiota shift with depression, autism, schizophrenia, substance use disorders, modulating gut permeability.**
  - Cenit MC et al. Influence of gut microbiota on neuropsychiatric disorders. World J Gastroenterol. 2017 Aug 14;23(30):5486-5498;
  - Walsh J et al. Drug-gut microbiota interactions: implications for neuropharmacology.Br J Pharmacol. 2018 May 21.
- **Weak evidence that probiotics reduce depressive symptoms (one of three double-blind studies)**
  - Wallace CJK, Milev R. The effects of probiotics on depressive symptoms in humans: a systematic review. Ann Gen Psychiatry. 2017 Feb 20;16:14
  - Romijn AR et al A double-blind, randomized, placebo-controlled trial of Lactobacillus helveticus and Bifidobacterium longum for the symptoms of depression. Aust N Z J Psychiatry. 2017 Aug;51(8):810-821
- **Probiotics might prevent rehospitalization for mania**
  - Dickerson F et al. Adjunctive probiotic microorganisms to prevent rehospitalization in patients with acute mania: A randomized controlled trial. Bipolar Disord. 2018 Apr 25. doi: 10.1111/bdi.12652. [Epub ahead of print]

Gut Microbiome: Bottom Lines

- We know very little
- Probiotics probably “couldn’t hurt”
- Yogurt is probably good for you
- Fecal transplants are not ready for psychiatric practice

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Stem Cell Therapy

- Experimental trials in Alzheimer's Disease, Erectile Dysfunction
- Preliminary experiments and musings concerning:
  - 3D brain "organoid" "minibrains" -
  - Alzheimer's disease, Autism, Schizophrenia, Bipolar Disorder

- Lee CT et al 3D brain Organoids derived from pluripotent stem cells: promising experimental models for brain development and neurodegenerative disorders. J Biomed Sci. 2017 Aug 20;24(1):59.
- Capogrosso P et al. Phase I and phase II clinical trials for the treatment of male sexual dysfunction-a systematic review of the literature. Expert Opin Investig Drugs. 2018 Jul;27(7):583-593.
- Duncan T, Valenzuela M. Alzheimer's disease, dementia, and stem cell therapy. Stem Cell Res Ther. 2017 May 12;8(1):111.
- Watmuff B et al. Stem cell-derived neurons in the development of targeted treatment for schizophrenia and bipolar disorder. Pharmacogenomics. 2017 Apr;18(5):471-479.

Medical Cannabinoids for Psychiatric Indications?

JAMA systematic review

- **Moderate-quality evidence –**for chronic pain and spasticity**.**
- **Low-quality evidence –** for nausea and vomiting due to chemotherapy, weight gain in HIV infection, sleep disorders, and Tourette syndrome.
- **Increased risk of short-term Adverse Events including serious AEs** (Common AEs included dizziness, dry mouth, nausea, fatigue, somnolence, euphoria, vomiting, disorientation, drowsiness, confusion, loss of balance, and hallucination.)

Whiting PF et al. Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. JAMA. 2015 Jun 23-30;313(24):2456-73

Medical Cannabinoids for Psychiatric Indications?

- **Anorexia Nervosa: Several negative clinical trials and meta-analysis.**
  - Contreras T et al. Do cannabinoids constitute a therapeutic alternative for anorexia nervosa? Medwave. 2017 Dec 1;17(9):e7095.
- **PTSD: Research is limited. Nabilone *may* reduce PTSD associated nightmares and improve sleep among patients with chronic pain. Thus-far known risks outweigh unknown benefits.**
  - Steenkamp MM et al. Marijuana and other cannabinoids as a treatment for posttraumatic stress disorder. Depress Anxiety. 2017; 34:207-216;
  - Babson KA et al. Cannabis, Cannabinoids, and Sleep. Curr Psychiatry Rep. 2017; 19:23
- **Dementia: Case reports and open label trials indicate possible benefit of adjunctive synthetic cannabinoids to reduce agitation, aberrant motor behavior and nighttime behavior.**
  - Weier M, Hall W. The Use of Cannabinoids in Treating Dementia.Curr Neurol Neurosci Rep. 2017; 17:56.

Medical Cannabinoids for Psychiatric Indications?

- **Insomnia:** Weak evidence, few studies.
- **Possible benefits for CBD for REM sleep behavior disorder and excessive daytime sleepiness,**
  - Babson KA et al. Cannabis, Cannabinoids, and Sleep: a Review of the Literature. Curr Psychiatry Rep. 2017; 19:23.
- **Schizophrenia – Very modest impact on positive but not negative symptoms.**
  - McGuire P et al. Cannabidiol (CBD) as an Adjunctive Therapy in Schizophrenia: A Multicenter Randomized Controlled Trial. Am J Psychiatry 2017; 175:225-231

Hallucinogens: Psilocybin

- **May decrease depression and anxiety symptoms in cancer-related psychiatric distress for months following a single administration** (3 controlled trials).
- **Treatment-resistant depression: Reductions in depression and anxiety symptoms 3 months after two doses** (small open-label study).
- **Promising for tobacco and alcohol addiction** (small open-label studies).

- Johnson MW, Griffiths RR. Potential Therapeutic Effects of Psilocybin. Neurotherapeutics. 2017; 14:734-74.
- Rucker JJ, et al. Psychedelics in the treatment of unipolar mood disorders: a systematic review. J Psychopharmacol. 2016; 30):1220-1229.
- Carhart-Harris RL et al. Psilocybin with psychological support for treatment-resistant depression: six-month follow-up. Psychopharmacology (Berl). 2018; 235:399-408.

Hallucinogens: MDMA (Ecstacy)

- **PTSD: Possible benefits for MDMA assisted psychotherapy for PTSD,** (several small phase II clinical trials with large effect sizes (0.9)).
- **Preliminary work in other anxiety, alcohol use, mood and eating disorders.**

- Feduccia AA Progress and promise for the MDMA drug development program. Psychopharmacology (Berl). 2018; 235:561-571.
- Mithoefer M (2017) A Manual for MDMA-Assisted Psychotherapy in the Treatment of Posttraumatic Stress Disorder; Version 8.1. https:// s3-us-west-1.amazonaws.com/mapscontent/research-archive/ mdma/TreatmentManual_MDMAAssistedPsychotherapyVersion+ 8.1_22+Aug2017.pdf

Hallucinogens: LSD, others

- **Anxiety associated with life-threatening disease: anxiety reduced for 2 months after two doses of LSD** (randomized controlled trial; 12 pts.)
  - Liechti ME. Modern Clinical Research on LSD. Neuropsychopharmacology. 2017; 42:2114-2127
- **Adverse Effects: Overall incidence of psychotic episodes appears to be rare in both ritual and recreational/noncontrolled settings.**
  - Dos Santos RG et al. Ayahuasca, dimethytryptamine, and psychosis: a systematic review of human studies. Ther Adv Psychopharmacol. 2017;7:141-157.

Herbals

- **Omega-3 polyunsaturated fatty acids**: reduced risk of progression to psychotic disorder and psychiatric morbidity over 6.7 yr follow-up in young people with subthreshold psychotic states (12-week randomized, double-blind, placebo-controlled trial).
  - Amminger GP et al. Longer-term outcome in the prevention of psychotic disorders by the Vienna omega-3 study. Nat Commun. 2015; 6:7934.
- **Chamomile:** 1600 mg/day of chamomile (approximately 4-5 cups of tea) -> 58% reduction in GAD (response), comparable to conventional anxiolytics, fewer adverse effects (8 week open study).
  - Keefe JR et al. Short-term open-label chamomile (Matricaria chamomilla L.) therapy of moderate to severe generalized anxiety disorder. Phytomedicine. 2016,15:1699-1705

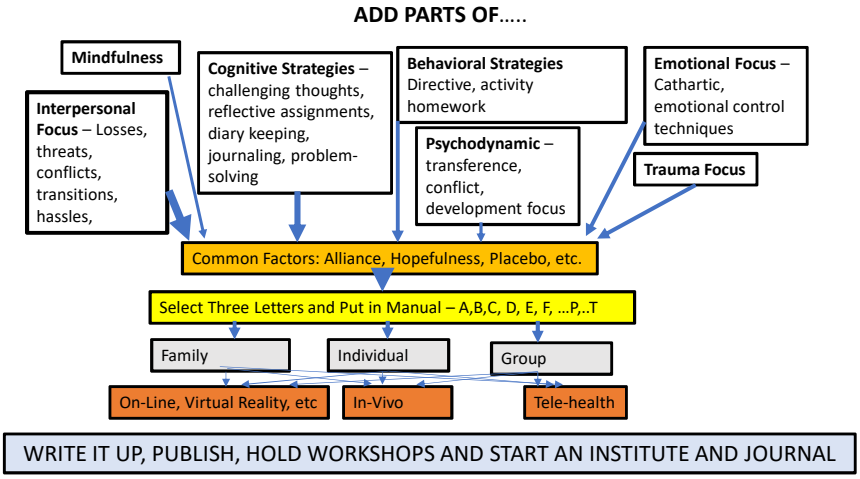
Etc.

- **Manipulating light:**
  - **Blue-blocking glasses reduce symptoms of mania**
  - **Noon-time bright light for bipolar depression**
- **Manipulating heat**
  - **Whole body hyperthermia to 38.5 C (101.3 F)**

- Henriksen TE et al. Blue-blocking glasses as additive treatment for mania: a randomized placebo-controlled trial. Bipolar Disord. 2016;18:221-32.
- Sit DK, et al. Adjunctive Bright Light Therapy for Bipolar Depression: A Randomized Double-Blind Placebo-Controlled Trial. Am J Psychiatry. 2018;175:131-139.
- Janssen CW et al. Whole-Body Hyperthermia for the Treatment of Major Depressive Disorder:Randomized Clinical Trial. JAMA Psychiatry. 2016; 73:789-95.

Interpersonal and Psychotherapeutic Treatments and Strategies

How do you grow a new psychotherapy?



New Interpersonal and Psychotherapeutic Treatments and Strategies – Examples

- **Non-Trauma Focused treatments for PTSD**
  - Interpersonal Psychotherapy (Am J Psychiatry. 2015;172:430-40.)
  - Present-Centered Therapy (J Trauma Stress 2014; 27:1–8.)
  - Mantram Therapy (Am J Psychiatry. 2018 Jun 20, e-ahead of print; doi: 10.1176/appi.ajp.2018.17060611.)
- **Brief therapies for PTSD**
  - Written Exposure Therapy (JAMA Psychiatry. 2018; 75: 233–239.)

Technologies

- **Telemedicine-TeleBehavioral Health?**
  - Collaborative Care and Integrated Behavioral Medicine
  - Yellowlees P, Shore J. **Telepsychiatry and Health Technologies**: A Guide for Mental Health Professional. American Psychiatric Press, 2018
- **Apps for Mental Health?**
  - Ask John Torous, Stephen Chan, John Luo (APA Smartphone App Workgroup) https://www.psychiatry.org/psychiatrists/practice/mental-health-apps.
  - Torous J et al. A Hierarchical Framework for Evaluation and **Informed Decision Making Regarding Smartphone Apps** for Clinical Care. Psychiatr Serv.2018; 69:498-500.

Technologies

- **Computer Assisted Treatments and Technology-Assisted Psychotherapy?**
  - Imel ZE et al. **Technology-enhanced human interaction** in **psychotherapy**. J Couns Psychol. 2017; 64:385-393;
  - Nesvåg S, McKay JR. Feasibility and Effects of **Digital Interventions to Support People in Recovery From Substance Use Disorders**. J Med Internet Res. 2018 Aug 23;20(8):e255.
- **Virtual Reality**
  - Mischkind MC (at CU!) et al. Review of **Virtual Reality Treatment in Psychiatry**: Evidence Versus Current Diffusion and Use. Curr Psychiatry Rep. 2017;19:80.
- **Wear-able Sensors and Wear-able Aids- "Digital Phenotyping" via Ecological Momentary Assessments**
  - Sahin NT et al. Second Version of **Google Glass** as a Wearable Socio-Affective Aid: Positive School Desirability, High Usability, and Theoretical Framework in a Sample of Children with Autism. JMIR Hum Factors. 2018 4; 5:e1.;
  - Wang Y et al. **Wrist-Worn Alcohol Biosensors**: Strengths, Limitations, and Future Directions. Alcohol. 2018;. [Epub ahead of print];
  - Torous J et al. New dimensions and new tools to realize the potential of RDoC: **digital phenotyping via smartphones** and connected devices. Transl Psychiatry. 2017; 7:e1053.

Technologies

- **"Gamification" – Serious Games for Mental Disorders**
  - Shah A et al. Developing **Digital Intervention Games for Mental Disorders.** Games Health J. 2018; 7:213-224;
  - Eichenberg C et al. **Serious Games for Psychotherapy.** Games Health J. 2017;6: 127-135;
  - Villani D et al. **Videogames for Emotion Regulation**. Games Health J. 2018; 7: 85-99.
- **AI Diagnosticians and Prognosticators?**
  - Massachusetts Institute of Technology. "Model can more naturally detect depression in conversations: **Neural network learns speech patterns that predict depression in clinical interviews**." ScienceDaily. ScienceDaily, 30 August 2018.<www.sciencedaily.com/releases/2018/08/180830180113.htm>.
  - Lee Y et al. Applications of **machine learning algorithms to predict therapeutic outcomes in depression**: A meta-analysis and systematic **review**. J Affect Disord. 2018; 241:519-532
  - Hoppe S et al. **Eye Movements** During Everyday Behavior Predict **Personality Traits**. Front Hum Neurosci. 2018 Apr 13;12:105.

Technologies

- **AI Therapists and Social Robots?**
  - Kleber S. **3 Ways AI Is Getting More Emotional** Harvard Business Review, July 2018; Miner AS et al. **Talking to Machines About Personal Mental Health Problems**. **JAMA**. 2017;318:1217-1218;
  - Huijnen C et al. Roles, Strengths and Challenges of Using **Robots in Interventions for Children with Autism Spectrum Disorder (ASD).** J Autism Dev Disord. 2018 Jul 17.[Epub ahead of print];
  - Góngora Alonso S et al. **Social Robots for People with Aging and Dementia:** A Systematic Review of Literature Telemed J E Health. 2018 Aug 23. [Epub ahead of print]
- **How long until Siri and Alexa offer CBT – or Psychoanalysis?**
- **How long before EPIC scans upcoming clinic schedules and offers curated reading recommendations before patient visits?**

Multi-Modal Systems-based Strategies

(Meta-Community Mental Health)

- **Comprehensive Care for First Episode Schizophrenia**
  - Kane JM et al. Comprehensive Versus Usual Community Care for First-Episode Psychosis: 2-Year Outcomes From the NIMH RAISE Early Treatment Program. Am J Psychiatry. 2016 Apr 1;173(4):362-72.
- **Managing Suicidal Patients following Hospital or ED Visits**
  - **Stanley B et al (Lisa Brenner).** Comparison of the Safety Planning Intervention With Follow-up vs Usual Care of Suicidal Patients Treated in the Emergency Department. JAMA Psychiatry 2018; Sept75(9):894-900.
- **Managing Alcohol and Substance Use Disorders.**
  - Barnett NP, et al. A preliminary randomized controlled trial of **contingency management** for **alcohol** use reduction **using a transdermal alcohol sensor**. Addiction. 2017; 112:1025-1035.
  - Kiluk BD et al. Randomized Clinical Trial of **Computerized and Clinician-Delivered CBT in Comparison With Standard Outpatient Treatment for Substance Use Disorders**: Primary Within-Treatment and Follow-Up Outcomes. Am J Psychiatry 2018; 175:853-863.

Future Multi-Modal Systems-Based Strategies?

- **Uber-care**
  - **24/7 availability on your smartphone?**
    - Hulsbosch AM et al. Videoconferencing in a mental health service in The Netherlands: A randomized controlled trial on patient satisfaction and clinical outcomes for outpatients with severe mental illness. J Telemed Telecare. 2017 Jun;23(5):513-520.
  - **Variable pricing based on time/convenience?**
  - **Cross-national tele-therapy?**
    - Mucic D. International **telepsychiatry**: a study of patient acceptability. J Telemed Telecare. 2008;14:241-3.
- **YouTube therapy**
  - **Personal and family psychoeducation**
  - **MOOC**

New Diagnostics

On the Horizon ... but not there yet

- **Pharmacogenetics and Pharmacoepigenetics** (i.e. genomic, proteomic, transcriptomic, metabolomic and other "omic" biomarkers)
  - Mora C et al. Expert Rev Mol Diagn. 2018; 18:513-529.
- **Connectome imaging biomarkers**
  - Finn ES, et al Dialogues Clin Neurosci. 2016; 18:277-287, Drysdale AT at al.. Nat Med. 2017; 23:28-38; Fischer AS et al. Biol Psychiatry Cogn Neurosci Neuroimaging. 2016; 1:262-270.
- **RDoC** (Research Domain Criteria)
  - Yager J, Feinstein RE.. J Clin Psychiatry. 2017; 78:423-432.
- **HiTOP** (Hierarchical Taxonomy of Psychopathology)
  - Kotov R et al. J Abnorm Psychol. 2017; 126:454-477.
- **Artificial Intelligence Data Mining**
  - Sun D Adv Exp Med Biol. 2017;1010:203-215.

SELF-ASSESSMENT QUESTIONS

SA-Q#1. Which of the following best contributes to the dissemination of treatment innovations?

A. Opinion leaders
B. Peer behavior
C. Institutional directives, prompts and guidelines
D. Aggressive detailing

SA-Q#2. Which of the following does not have any FDA approval as a neuromodulatory intervention?

A. Electro-convulsive therapy (ECT)
B. Deep Brain Stimulation (DBS)
C. Vagal Nerve Stimulation (VNS)
D. Transcranial Direct Current Stimulation (TDCS)
E. Repetitive Transcranial Magnetic Stimulation (rTMS)

SA-Q#3. In randomized controlled trials of cannabidiol (CBD) as an adjunctive agent for the treatment of schizophrenia, CBD has been shown to have which of the following properties?

A. Strongly reduces negative symptoms but has no impact on positive symptoms.
B. Modestly improves positive symptoms but not negative symptoms.
C. Has no effect on either positive or negative symptoms.
D. Strongly worsens both positive and negative symptoms.
E. Worsens positive symptoms, but benefits negative symptoms.

SA-Q#4. Which of the following has been combined with manualized psychotherapy in formal treatment studies for PTSD?

A. Propranolol
B. Methylenedioxymeth-amfetamine (MDMA- Ecstasy)
C. Marijuana
D. Nicotine
E. Mementine

SA-Q#5. In experiments using Google Glass in the adjunctive treatment of youth with autism spectrum disorder, interventions are attempting to assist patients with which of the following functions?

A. to speak.
B. to read
C. to interpret emotions on other people's faces
D. to practice emotional self-control
E. to use the internet

TABLETOP BRAINSTORM DISCUSSION

(for groups of three, one to serve as scribe)

Flip a coin

HEADS: tackle 1 and 2 ***TAILS: tackle 3 and 4***

Flip coin – Heads: tackle 1 and 2; Tails: tackle 3 and 4.

1. What 3+ psychiatric and mental health problems come to your attention for which you're least likely to see improvement or achieve good outcomes?
2. What 3+ currently unavailable resources might best help in those situations?
3. What 3+ new, emerging or different specific interventions (biological, psychosocial, technological and/or systems-based strategies) would most likely improve your overall outcomes?
4. What 3+ concrete steps could you and your immediate workgroup – or the larger organization – take to help your top 3 choices for new interventions or strategies become available or realities?

Thanks for listening…..

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