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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

TOP ARTICLES OF THE YEAR

UW PACC PANELISTS

12/12/2024

SPEAKER DISCLOSURES

✓ Any conflicts of interest?

Planner disclosures

The following series planners have no relevant conflicts of interest to disclose; other disclosures have been mitigated.

Mark Duncan MD

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OBJECTIVES

1. Highlight some of the top articles that have stood out to us over the past 12 months.

2. Describe the main learning points we want to share from those articles.

3. Address some of the limitations of those articles and resources.

KARI'S ARTICLE OF THE YEAR 2024

KARI A. STEPHENS, PHD

PSYCHOLOGIST, VICE CHAIR OF RESEARCH

PROFESSOR, UW DEPT OF FAMILY MEDICINE

UW Medicine
UW SCHOOL OF MEDICINE

Integrated Care Training Program
UW Psychiatry & Behavioral Sciences

project ECHO

Associations of intervention completion in a pragmatic trial on integrated behavioral health (IBH) and patient outcomes

Kari A. Stephens, PhD
Constance van Eeghen, PhD
Zihan Zheng, MS
Tracy Anastas, PhD
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Maria G. Prado, MPH
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Rodger Kessler, PhD

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FAMILY MEDICINE

LEARNING OBJECTIVES

- **Describe** a primary care practice-centric intervention aimed at improving integrated behavioral health for patients with multiple chronic conditions.

- **Describe** how the stages of completion for IBH-PC Toolkit intervention were associated with practice and patient level outcomes for patients with multiple chronic conditions.

Trials

STUDY PROTOCOL

Open Access

Integrating Behavioral Health and Primary Care (IBH-PC) to improve patient-centered outcomes in adults with multiple chronic medical and behavioral health conditions: study protocol for a pragmatic cluster-randomized control trial

Abigail M. Crocker[1*] , Rodger Kessler[2,3], Constance van Eeghen[1], Levi N. Bonnell[1], Ryan E. Breshears[4], Peter Callas[1], Jessica Clifton[1], William Elder[5], Chet Fox[6], Sylvie Frisbie[1], Juvena Hitt[1], Jennifer Jewiss[1], Roger Kathol[7], Kelly Clark/Keefe[1], Jennifer O'Rourke-Lavoie[1], George S. Leibowitz[8], C. R. Macchi[2], Mark McGovern[9], Brenda Mollis[10], Daniel J. Mullin[11], Zsolt Nagykaldi[12], Lisa Watts Natkin[1], Wilson Pace[13], Richard G. Pinckney[1], Douglas Pomeroy[1], Alexander Pond[1], Rachel Postupack[14], Paula Reynolds[1], Gail L. Rose[1], Sarah Hudson Scholle[15], William J. Sieber[16], Terry Stancin[17], Kurt C. Stange[18], Kari A. Stephens[10], Kathryn Teng[17], Elizabeth Needham Waddell[19] and Benjamin Littenberg[1]

IBH-PC

- **$18.5M PCORI funded**

- **2-arm, parallel, superiority, pragmatic cluster-randomized trial**

- **Intervention = quality improvement and lean-based intervention to improve integrated behavioral health for patients with multiple chronic conditions**

Integrating Behavioral Health and Primary Care for Comorbid Behavioral and Medical Problems

BH PC

Condition or disease ❶
Arthritis
Asthma
Chronic Obstructive Lung Disease
Diabetes
Heart Failure
Hypertension
Anxiety
Chronic Pain
Depression
Fibromyalgia
Insomnia
Irritable Bowel Syndrome
Problem Drinking
Substance Use Disorder

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IBH-PC PRIMARY RESEARCH QUESTIONS

1. *Does using the IBH-PC toolkit, a practice-level intervention, affect patient-centered outcomes in adults with multiple chronic medical and behavioral health conditions?*

2. *Does using the IBH-PC toolkit affect the degree of practice-level behavioral health care integration in primary care practices?*

3. *What factors support or impede successful integration of behavioral health care into primary care practices?*

4. *What are the costs of implementing the IBH-PC toolkit?*

THIS STUDY…

1. *Does using the IBH-PC toolkit, a practice-level intervention, affect patient-centered outcomes in adults with multiple chronic medical and behavioral health conditions?*

2. *Does using the IBH-PC toolkit affect the degree of practice-level behavioral health care integration in primary care practices?*

Tested our hypothesis: Practices that completed <u>more stages</u> in the intervention arm would report <u>higher levels of integration</u> and patients in these practices would report <u>greater improvement in their physical and mental health</u> over time

Stephens, K. A., van Eeghen, C., Zheng, Z., Anastas, T., Ma, K. P. K., Prado, M. G., Clifton, J., Rose, G., Mullin, D., Chan, K. C. G., & Kessler, R. (in press). Associations of intervention stage completion on practice level of integrated behavioral health and behavioral health outcomes in an integrated behavioral health and primary care randomized pragmatic intervention trial. *Annals of Family Medicine.*

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IBH CORE PROCESSES & STRUCTURES:

PRINCIPLES (5) – 25 PROCESSES, 9 STRUCTURES

Patient-centric Care	Treatment to Target	Use of EBTs	Conduct Efficient Team Care	Population Based Care	Structures Needed to Support IBH
• Orient patient • Shared decision making • Patient autonomy • Changes in symptoms / function	• Target health and quality of life • Stepped care • Goal setting • Assessment • Barriers • Outcomes • Tracking system • Caseload management	• Coordinate evidence-based treatments • Use evidence-based treatments • Psycho-education	• Roles and workflow • Brief visits • Team communication • Team trust • Common language • Fast and easy access • Psychiatric consultation / care	• Resources target those most in need • Triage processes	• Financial billing sustainability • Administrative support and supervision • Quality improvement • EHR • Clinic space • Behavioral Health Provider • Protected time • Accountability • Tracking system for panel management

Stephens, K. A., van Eeghen, C., Mollis, B., Au, M., Brennhofer, S., Martin, M., Clifton, J., Witwer, E., Hansen, A., Monkman, J., Buchanan, G., & Kessler, R. (2020). Defining and Measuring Core Processes and Structures in Integrated Behavioral Health in Primary Care: A Cross-Model Framework. *Translational Behavioral Medicine, 10,* 527-538. PMCID: PMC8128511

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METHODS

> **Practices:**
>> – **>= 1 primary care provider**
>> – **Co-located licensed behavioral health provider >= .5 FTE with shared electronic health record system**
>> – **Willing to provide (EHR) data, be randomized, complete study measures**

> **Patients:**
>> – **>= 18**
>> – **Seen at least twice in last 24 months at the practice**
>> – **Either had:**
>>> **>= 1 eligible chronic medical condition AND >= 1 chronic behavioral health condition
OR >=3 chronic medical conditions**

> **Practice were randomized to 2 arms – treatment as usual vs. IBH-PC intervention**

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IBH-PC Trial: Intervention

https://sites.google.com/view/ibhpc/home
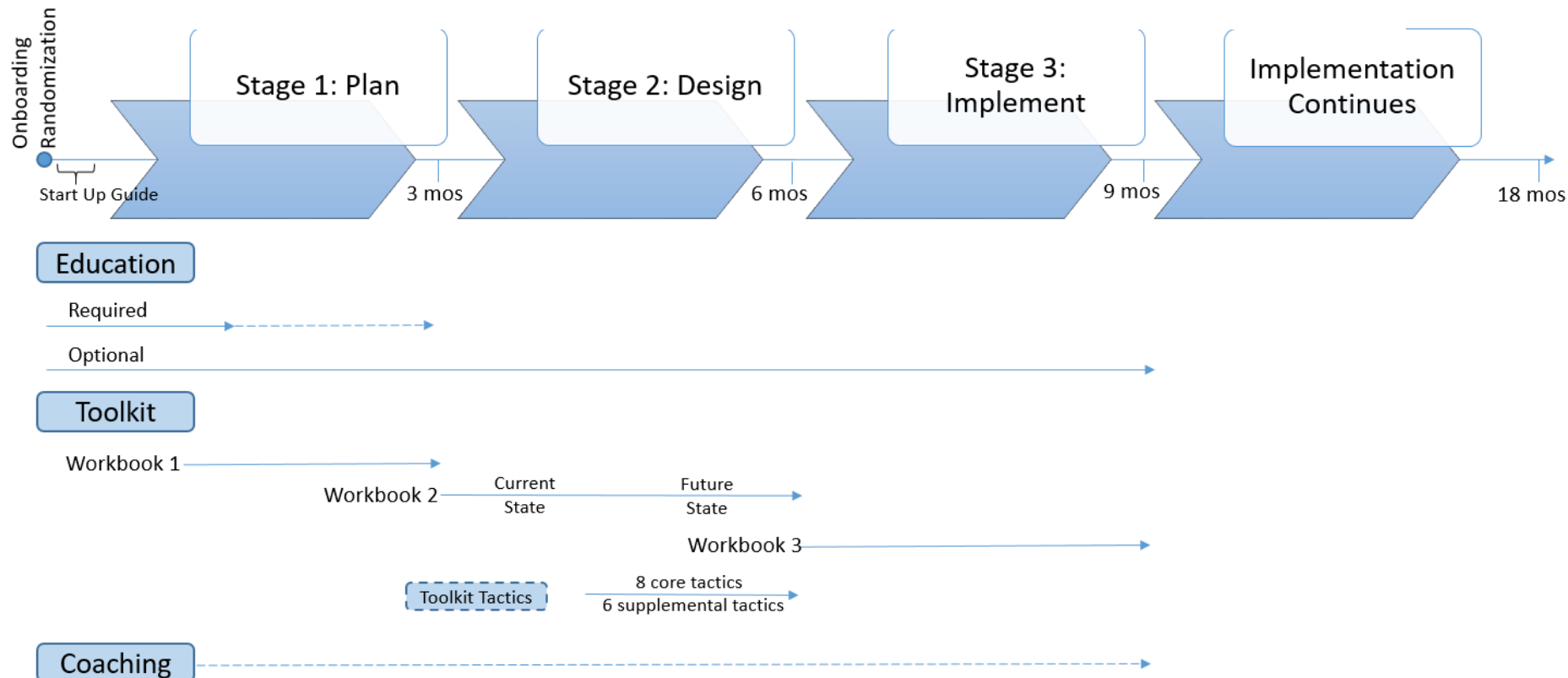
- **Toolkit:** 3 stages based on a QI lean approach

- **Education:** 70 asynchronous modules for ALL members of the primary care team

- **Coaching:** complex change process supported by dual expertise in lean management and psychology

PATIENT OUTCOMES

- Anxiety
- Depression
- Fatigue
- Sleep disturbance
- Pain interference and intensity
- Social participation
- Physical function

PROMIS 29 2.0 (T-score)

- physical function
- anxiety
- depression
- fatigue
- sleep disturbance
- social participation
- pain interference in the past seven days

PHQ-9 (0-27)

- Patient Health Questionnaire measures depression symptoms

GAD-7 (0-21)

- Generalized Anxiety Disorder scale measures anxiety symptoms

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PRACTICE OUTCOME = LEVEL OF INTEGRATION

Practice Integration Profile v1.0

- Scores range from 0 (no integration) to 100 (full integration)

- 30 items

6 domains:

- practice workflow
- clinical services
- integration methods
- case identification
- patient engagement
- workspace arrangement and infrastructure

>=4 people at each practice filled out the PIP

- medical primary care provider (PCP)
- BHP
- administrator such as a clinic manager
- provider or staff of the practice's choice)

ANALYSES

Multilevel mixed-effects models were conducted using the number of intervention stages completed as the primary exposure of interest. Baseline outcome measurement, as well as the time interval from baseline to midpoint and follow-up measurements, respectively, were adjusted for in all analyses.

Patient :
3-level mixed models with repeated (midpoint and 2-year follow-up) measurements (level 1) nested in patients (level 2) nested in individual primary care practices (level 3)

- Only patients with room for improvement were analyzed
- Adjusted for age, sex, race, ethnicity, employment status, living region (urban/rural), and insecurity status (>=1 housing, food, or financial)

Practice:
3-level mixed models with repeated (midpoint and 2-year follow-up) measurements (level 1) nested in staff/providers (level 2) nested in primary care practices (level 3)

- Adjusted for the ratio of BHP FTE:PCP FTE, baseline outcome measurement, as well as the time interval from baseline to midpoint and follow-up measurements
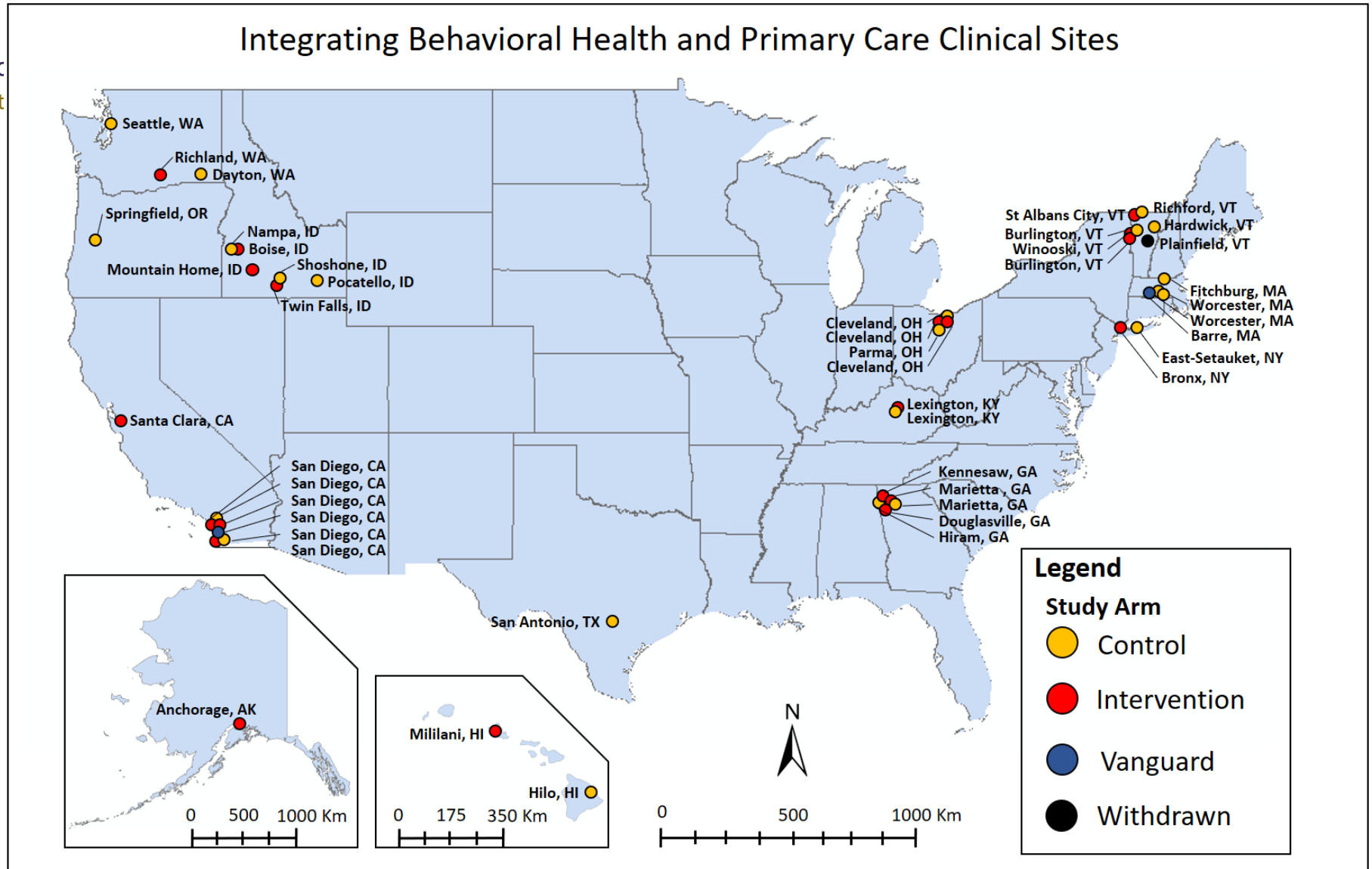
CONSORT DIAGRAM – 2017-2020

Practice-level Analysis

Randomized practices
(n=42 with n=237 providers and staff)

Active practices
(n=20 with n=116 providers and staff)

Control practices
(n=22 with n=121 providers and staff)

Patient-level Analysis

Randomized practices
(n=41 with n=2,945 eligible patients)

Active practices
(n=19 with n=1,190 eligible patients)

Control practices
(n=22 with n=1,755 eligible patients)

PATIENT CHARACTERISTICS

- 46.3% married/living as married

- 29.8% disabled or unemployed

- 62.1% household income <$50k

- 54.4% high school education or below

	Overall (N=2945)	Active Site (N=1190)	Control Site (N=1755)	p-value
Age, years	61.8 (13.3)	61.7 (12.8)	61.8 (13.6)	0.90
Sex				0.11
Female	1884 (64.0%)	742 (62.4%)	1142 (65.1%)	
Male	1054 (35.8%)	448 (37.6%)	606 (34.5%)	
Race				0.001*
White	2215 (75.2%)	849 (71.3%)	1366 (77.8%)	
Black or African American	356 (12.1%)	160 (13.4%)	196 (11.2%)	
American Indian or Alaskan Native	30 (1.0%)	12 (1.0%)	18 (1.0%)	
Asian	94 (3.2%)	51 (4.3%)	43 (2.5%)	
Native Hawaiian/Other Pacific Islander	42 (1.4%)	23 (1.9%)	19 (1.1%)	
Other/Prefer not to say	202 (6.9%)	91 (7.6%)	111 (6.3%)	
Ethnicity				0.70
Hispanic	240 (8.1%)	103 (8.7%)	137 (7.8%)	
Non-Hispanic	2660 (90.3%)	1068 (89.7%)	1592 (90.7%)	
Prefer not to say	29 (1.0%)	12 (1.0%)	17 (1.0%)	

PATIENT CHRONIC CONDITIONS – TOP 5

- **>80% had chronic pain or hypertension**

- **48.1% depression**

- **45.3% diabetes**

- **41.1% arthritis**

- **34.5% anxiety**

- **Mean # of total conditions = 4.4 (SD = 1.7)**

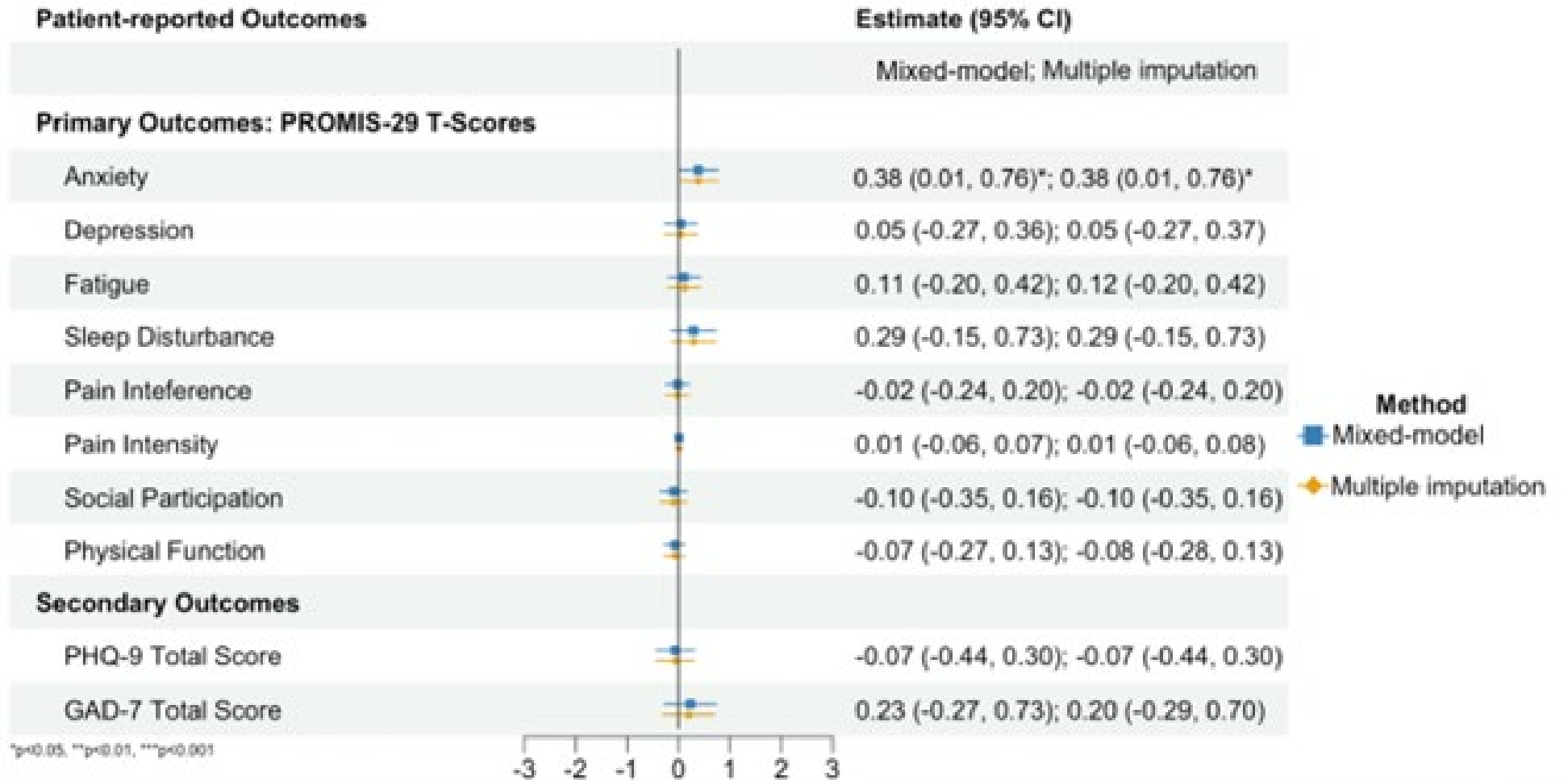UNIVERSITY *of* WASHINGTON

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PRACTICE CHARACTERISTICS

- Most were Family Medicine or mixed Family and Internal Medicine practices

- Mean # of BHPs 1.5 (SD = 1.1)

- Mean # of PCPs = 6.0 (SD = 0.26)

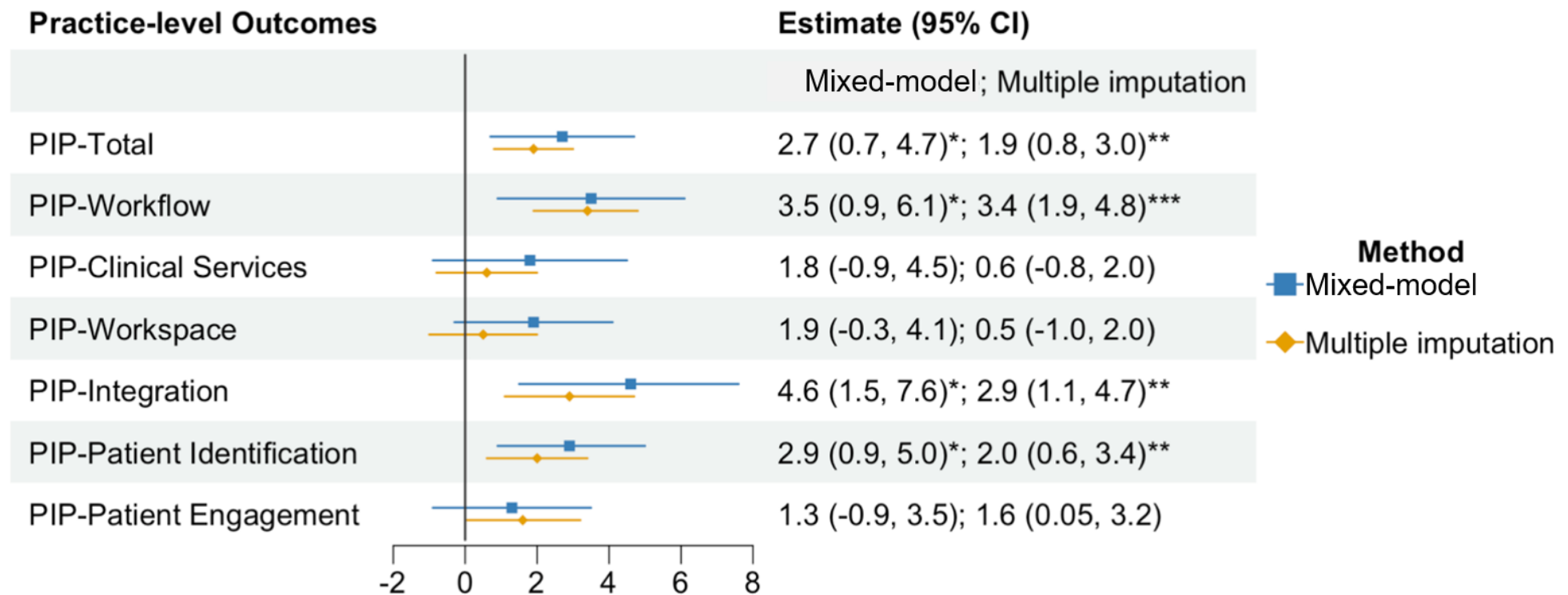|	Overall (N = 42)	Intervention Arm (n = 20)	Control Arm (n = 22)	p-value
Practice specialty				0.85
Internal medicine	7 (17%)	3 (15%)	4 (18%)	
Family medicine	20 (48%)	9 (45%)	11 (50%)	
Mixed	15 (36%)	8 (40%)	7 (32%)	
Organization type				
Community Health Center	15 (36%)	8 (40%)	7 (32%)	0.82
Hospital	20 (48%)	10 (50%)	10 (45%)	0.77
Private	4 (10%)	1 (5%)	3 (14%)	0.67
Academic	19 (45%)	10 (50%)	9 (41%)	0.78
Resident training site	16 (38%)	9 (45%)	7 (32%)	0.58
Non-profit	37 (88%)	19 (95%)	18 (82%)	0.40
Geographic region				0.88
Pacific Northwest	3 (7%)	1 (5%)	2 (9%)	
Mountain	8 (19%)	4 (20%)	4 (18%)	
The South	8 (19%)	4 (20%)	4 (18%)	
New England	9 (21%)	3 (15%)	6 (27%)	
Mid-Atlantic & Great Lakes	6 (14%)	3 (15%)	3 (14%)	
West Coast & Hawaii	8 (19%)	5 (25%)	3 (14%)	
Urban by RUCA	35 (83%)	18 (90%)	17 (77%)	0.49
County social deprivation index	44.9 (22.0)	46.4 (23.3)	43.5 (21.1)	0.68
Patient cared for by the practice each year	9285 (5066)	9138 (4549)	9419 (5599)	0.86
Baseline BHP FTE	1.5 (1.1)	1.7 (1.4)	1.3 (0.7)	0.18
Baseline PCP FTE	6.0 (3.2)	5.9 (2.7)	6.1 (3.6)	0.83
Baseline BHP FTE: PCP FTE	0.30 (0.26)	0.35 (0.28)	0.26 (0.24)	0.27

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RESULTS - PATIENTS

- No significant differences

- ** we were unable to account for service utilization

Patient-reported Outcomes	Estimate (95% CI)
	Mixed-model; Multiple imputation
Primary Outcomes: PROMIS-29 T-Scores	
Anxiety	0.38 (0.01, 0.76)*; 0.38 (0.01, 0.76)*
Depression	0.05 (-0.27, 0.36); 0.05 (-0.27, 0.37)
Fatigue	0.11 (-0.20, 0.42); 0.12 (-0.20, 0.42)
Sleep Disturbance	0.29 (-0.15, 0.73); 0.29 (-0.15, 0.73)
Pain Inteference	-0.02 (-0.24, 0.20); -0.02 (-0.24, 0.20)
Pain Intensity	0.01 (-0.06, 0.07); 0.01 (-0.06, 0.08)
Social Participation	-0.10 (-0.35, 0.16); -0.10 (-0.35, 0.16)
Physical Function	-0.07 (-0.27, 0.13); -0.08 (-0.28, 0.13)
Secondary Outcomes	
PHQ-9 Total Score	-0.07 (-0.44, 0.30); -0.07 (-0.44, 0.30)
GAD-7 Total Score	0.23 (-0.27, 0.73); 0.20 (-0.29, 0.70)

*p<0.05, **p<0.01, ***p<0.001

-3 -2 -1 0 1 2 3

Method
- Mixed-model
- Multiple imputation

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RESULTS - PRACTICE

- No significant differences

- ** we were unable to account for service utilization

Practice-level Outcomes	Estimate (95% CI)
	Mixed-model; Multiple imputation
PIP-Total	2.7 (0.7, 4.7)*; 1.9 (0.8, 3.0)**
PIP-Workflow	3.5 (0.9, 6.1)*; 3.4 (1.9, 4.8)***
PIP-Clinical Services	1.8 (-0.9, 4.5); 0.6 (-0.8, 2.0)
PIP-Workspace	1.9 (-0.3, 4.1); 0.5 (-1.0, 2.0)
PIP-Integration	4.6 (1.5, 7.6)*; 2.9 (1.1, 4.7)**
PIP-Patient Identification	2.9 (0.9, 5.0)*; 2.0 (0.6, 3.4)**
PIP-Patient Engagement	1.3 (-0.9, 3.5); 1.6 (0.05, 3.2)

Method
■ Mixed-model
◆ Multiple imputation

DISCUSSION

IBH-PC offers practices a flexible, practice-centric solution for busy, complex primary care practices to significantly increase overall level of behavioral health integration, as well as across workflow, integration methods, and patient identification domains

Changes were complex and practice-driven, and sustainability was likely interrupted due to the 2020 COVID pandemic at the end of the observation period, from May through December, 2020

Patient outcomes may not be apparent due to inability to account for whether or not patients were seen by their PCP or BHP after the intervention period

Conclusion: A practice-centric flexible intervention aimed at improving the level of IBH in primary care can help practices transform to meet these needs and improve the health of their most complex patients

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Thank you!

Questions?
Kari Stephens: Kstephen@uw.edu

Cognitive behavioral therapy in adults with functional seizures: A systematic review and meta-analysis of randomized controlled trials

Pierludovico Moro [a], Simona Lattanzi [b], Christoph P. Beier [c,d], Carlo Di Bonaventura [a,*], Emanuele Cerulli Irelli [a]

[a] Department of Human Neurosciences, Sapienza University, Rome, Italy
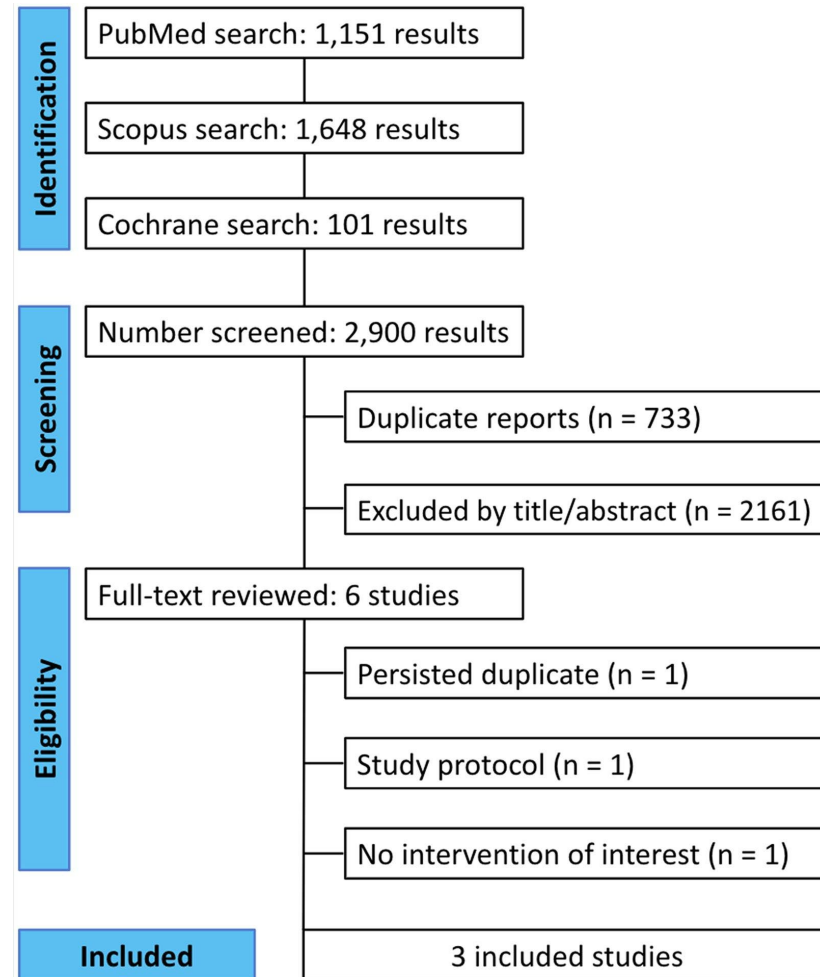[b] Neurological Clinic, Department of Experimental and Clinical Medicine, Marche Polytechnic University, Ancona, Italy
[c] Department of Neurology, Odense University Hospital, Odense, Denmark
[d] Department of Clinical Research, University of Southern Denmark, Odense, Denmark

FUNCTIONAL SEIZURE DISORDER

- Conversion Disorder
- Psychogenic Nonepileptic Seizure Disorder
- Dissociative Seizure Disorder
- Functional Dissociative Seizure Disorder

MORO ET AL 2024 META-ANALYSIS – PRISMA FLOWCHART

Identification

PubMed search: 1,151 results

Scopus search: 1,648 results

Cochrane search: 101 results

Screening

Number screened: 2,900 results

Duplicate reports (n = 733)

Excluded by title/abstract (n = 2161)

Eligibility

Full-text reviewed: 6 studies

Persisted duplicate (n = 1)

Study protocol (n = 1)

No intervention of interest (n = 1)

Included

3 included studies

Cognitive-behavioral therapy for psychogenic nonepileptic seizures

A pilot RCT

L.H. Goldstein, PhD, T. Chalder, PhD, C. Chigwedere, MSc, M.R. Khondoker, PhD, J. Moriarty, MD, B.K. Toone, MPhil, and J.D.C. Mellers, MRCPsych | AUTHORS INFO & AFFILIATIONS

Multicenter Pilot Treatment Trial for Psychogenic Nonepileptic Seizures
A Randomized Clinical Trial

W. Curt LaFrance Jr, MD, MPH[1,2,3]; Grayson L. Baird, MS[4,5,6]; John J. Barry, MD[7]; et al

≫ Author Affiliations | Article Information

Cognitive behavioural therapy for adults with dissociative seizures (CODES): a pragmatic, multicentre, randomised controlled trial

Laura H Goldstein, Emily J Robinson, John D C Mellers, Jon Stone, Alan Carson, Markus Reuber, Nick Medford, Paul McCrone, Joanna Murray, Mark P Richardson, Izabela Pilecka, Carole Eastwood, Michele Moore, Iris Mosweu, Iain Perdue, Sabine Landau*, Trudie Chalder*, on behalf of the CODES study group†

Summary

Background Dissociative seizures are paroxysmal events resembling epilepsy or syncope with characteristic features that allow them to be distinguished from other medical conditions. We aimed to compare the effectiveness of cognitive behavioural therapy (CBT) plus standardised medical care with standardised medical care alone for the

SUMMARY OF OUTCOMES

CBT versus standard medical treatment improved seizure frequency, anxiety, depression, and quality of life

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NEXT STEPS

Treatment Dissemination!

RIES FAVE ARTICLE 2024 UWPACC

- October 9, 2024

- **Comparative Effectiveness of Antipsychotics in Patients With Schizophrenia Spectrum Disorder**

- Aleksi Hamina, PhD (Pharm)[1,2]; Heidi Taipale, PhD (Pharm)[1,3]; Johannes Lieslehto, MD, PhD[1]; et alMarkku Lähteenvuo, MD, PhD[1]; Antti Tanskanen, PhD[1,3]; Ellenor Mittendorfer-Rutz, PhD[1,3]; Jari Tiihonen, MD, PhD[1,3]

- Author Affiliations Article Information

- **Design, Setting, and Participants-**

- **Schizophrenia Spectrum Disorders**

- **Swedish Healthcare System n=131,476**

- This comparative effectiveness research study with a within-individual analysis included data from Swedish health care registers of

- inpatient and specialized outpatient care, sickness absence, and disability pensions among all individuals aged 16 to 65 years who were diagnosed with schizophrenia spectrum disorder from January 1, 2006, to December 31, 2021, including an incident cohort and a prevalent cohort.

Main Outcomes and Measures

The risks for psychosis relapse hospitalization and treatment failure (psychiatric hospitalization, death, or change in an antipsychotic medication) were adjusted for the temporal order of treatments, time since cohort entry, and concomitant drugs.

Comparisons of all antipsychotics with oral olanzapine, the most commonly used antipsychotic, were investigated.

DEFINITIONS

- **Outcomes**
- The outcome of ==relapse== was defined as hospitalization due to psychosis (*ICD-10* codes F20-F29) and

- ==treatment failure== as a composite outcome of any of the following: psychiatric hospitalization (*ICD-10* codes F00-F99), death, or any change in antipsychotic medication (switch, discontinuation, or add-on of other antipsychotics).

QUESTION DO ANTIPSYCHOTICS DIFFER IN THEIR EFFECTIVENESS TO PREVENT RELAPSE AND TREATMENT FAILURE IN PATIENTS WITH SCHIZOPHRENIA SPECTRUM DISORDERS?

Findings In this comparative effectiveness research study including Swedish health care register data for 131,476 individuals, specific antipsychotics were compared with oral olanzapine.

Paliperidone 3-month long-acting injectable (LAI),
Aripiprazole LAI, olanzapine LAI, and clozapine were associated with
the lowest risks for relapse,

Lowest risks for treatment failure included the first 3 agents and paliperidone 1-month LAI;

in contrast, quetiapine was associated with the highest risk of relapse.

Detailed Results Among the full cohort of ==131 476== individuals, the mean (SD) age of the study cohort was 45.7 (16.2) years (70 054 men [53.3%]).

During a median follow-up of 12.0 years [IQR, 5.2-16.0 years], ==48.5% of patients (N = 63 730) experienced relapse and 71.1% (N = 93 464) underwent treatment failure at least once.==

Compared with oral olanzapine, paliperidone 3-month long-acting injectable (LAI) was associated with the lowest adjusted hazard ratio (AHR) in the prevention of relapses ==(AHR, 0.66; 95% CI, 0.51-0.86), followed by aripiprazole LAI (AHR, 0.77 [95% CI, 0.70-0.84]), olanzapine LAI (AHR, 0.79 [95% CI, 0.73-0.86]), and clozapine (AHR, 0.82== [95% CI, 0.79-0.86]).

Quetiapine was associated with the highest risk of relapse (AHR, 1.44 [95% CI, 1.38-1.51]).

For prevention of treatment failure,

paliperidone 3-month LAI was associated with the lowest AHR (AHR, 0.36 [95% CI, 0.31-0.42]),

followed by aripiprazole LAI (AHR, 0.60 [95% CI, 0.57-0.63]),

olanzapine LAI (AHR, 0.67 [95% CI, 0.63-0.72]), and

paliperidone 1-month LAI (AHR, 0.71 [95% CI, 0.68-0.74]).

QUESTIONS

- What is an AHR ?, what are problems with it?

- What about cost and access ?

- Others?

- *Thank you !!! For a great year.....And Happy Holidays*

Benzodiazepine Discontinuation and Mortality Among Patients Receiving Long-Term Benzodiazepine Therapy

Donovan T. Maust, MD, MS; Kierstdea Petzold, MS; Julie Strominger, MS; H. Myra Kim, ScD; Amy S. B. Bohnert, PhD, MHS

OVERVIEW

- Objective:
  - To ID the association of benzodiazepine discontinuation with mortality and other adverse events among patients on stable long-term benzodiazepine therapy.

- Methods: Retrospective Cohort
  - Used data from US commercial database (Optum) from 1/1/2013-12/31/2017.
  - Adults with stable long-standing benzodiazepine prescription
    - Long-standing: 90% of days of prescription during baseline year, with no prescription gaps > 30 days.
    - Stable: monthly average doses within 30% of the baseline mean
  - Benzo discontinuation: no benzodiazepine prescription coverage for 31 consecutive days identified during a 6-month grace period after baseline

RESULTS

- **Primary outcome**: mortality in benzo discontinuers vs continuers
  - Cumulative incidence of death
    - Discontinuers: 6.3% (CI 6.0-6.6%)
    - Continuers: 3.9% (CI 3.89-4.1%)

Mortality risk at 12 months for discontinuers 1.6 (CI 1.5-1.7) vs continuers

- **Secondary outcomes**: nonfatal OD, suicide attempt/ideation, ED visits
  - **All worse for discontinuers** (1.2 to 1.4x) vs continuers

- No difference in younger vs older patients
- Outcomes worse with recent opioid exposure (2.1 mortality risk)
- Not a consistent finding among other studies

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The American Journal of
Psychiatry

Long-Term Use of Benzodiazepines and Benzodiazepine-Related Drugs: A Register-Based Danish Cohort Study on Determinants and Risk of Dose Escalation

Thomas Wolff Rosenqvist, M.D., Marie Kim Wium-Andersen, M.D., D.M.Sc., Ida Kim Wium-Andersen, M.D., Ph.D.,
Martin Balslev Jørgensen, M.D., D.M.Sc., Merete Osler, M.D., D.M.Sc.

OVERVIEW

- Objective:
  - investigate the frequency and determinants of long-term use
  - risk of dose escalation of benzodiazepines and benzodiazepine-related drugs (z-drugs like zolpidem)

- Methods: Retrospective cohort
  - All Danish adults (20-80yo) living in Denmark from 1/1/2000 to 12/30/2020 were followed using their national prescription registry.
  - Long-term use: more than 1 year
  - Dose escalation: increase to a level above the recommended level
    - >40 Diazepam milligram equivalents for < 65yo
    - >20 Diazepam milligram equivalents if 65yo +

RESULTS

- **Overall risk of use for more than 1 year➔15% of those prescribed BZRAs**
  - Z-drugs: 17.8%
  - Anxiolytic benzos: 13.1%
  - Hypnotic benzos: 9.8%
- Risk was higher for use of z-drugs and anxiolytic benzos > 1 year in patients with psychiatric comorbidity
  - aOR: 1.24
- Comorbid SUD risk high for long-term use: aOR: 1.69

- Over the course of 7 years, most people stopped using BZRAs.
  - 3.3% of those using for 1 year continued to use over 7 years

RESULTS: DOSE ESCALATION

- **Only 7%** (N=3,545) of the approximately 5% of individuals with a continuous use over 3 years escalated in dose to a level above the recommended dosages

- Proportion of users who escalated their dose over 3 years
  - Hypnotic benzos: 13.6%
  - Z-drugs: 7.7%
  - Anxiolytic benzos: 5.2%%

- Psychiatric comorbidity was associated with the risk of dose escalation.
  - Hypnotic benzos: aOR 1.53
  - Anxiolytic benzos: aOR 1.26
  - Z-drugs: aOR 1.45

TAKEAWAYS

- Increased mortality can be a risk for benzo discontinuation
- Benzodiazepine and related drugs may infrequently lead to long-term use and dose escalation.
- Restricted BZRAs have been associated with increases in other sedating drugs: quetiapine, promethazine, and melatonin

Recommendation

- Prioritize choosing the "right med" based on evidence for effect, and balance the risks and benefits.
  - Benzodiazepines can be the "right med"