Revealing unknown benefits of existing medications to aid the discovery of new treatments for post-traumatic stress disorder

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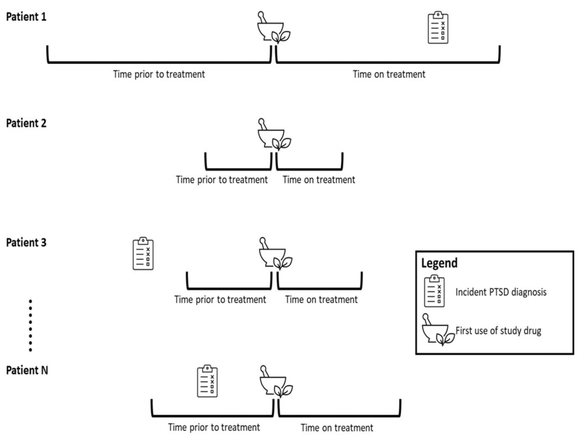
INTRO

There is a large unmet need for medications that are effective at preventing or treating post-traumatic stress disorder (PTSD). The two currently approved treatments in the US are antidepressants that are limited in their efficacy for treating the totality of symptoms associated with PTSD and do not prevent incidence of the condition. Real-world data can provide a way to identify new drug candidates and mechanisms of action for the development of new therapeutic options for the treatment of PTSD.

METHODS

A self-controlled cohort study design tested the association between 1399 medications and the incidence of PTSD across four US insurance claims databases. Medications associated with ≥30% reduction in risk of PTSD in ≥2 databases were identified. The incident rate ratios, 95% confidence intervals, and p-values were calibrated using negative controls to adjust for residual bias. Meta-analyses with random effects were used to pool results across databases.

Figure 1. The self-controlled cohort study



Example showing incident PTSD occurring during the time a patient was on treatment (Patient 1), not occurring in patient's history (Patient 2), occurring outside of the observation windows and therefore not counted in either period (Patient 3) and occurring during the unexposed control period (Patient N). This approach was repeated for all medications identified in the database.

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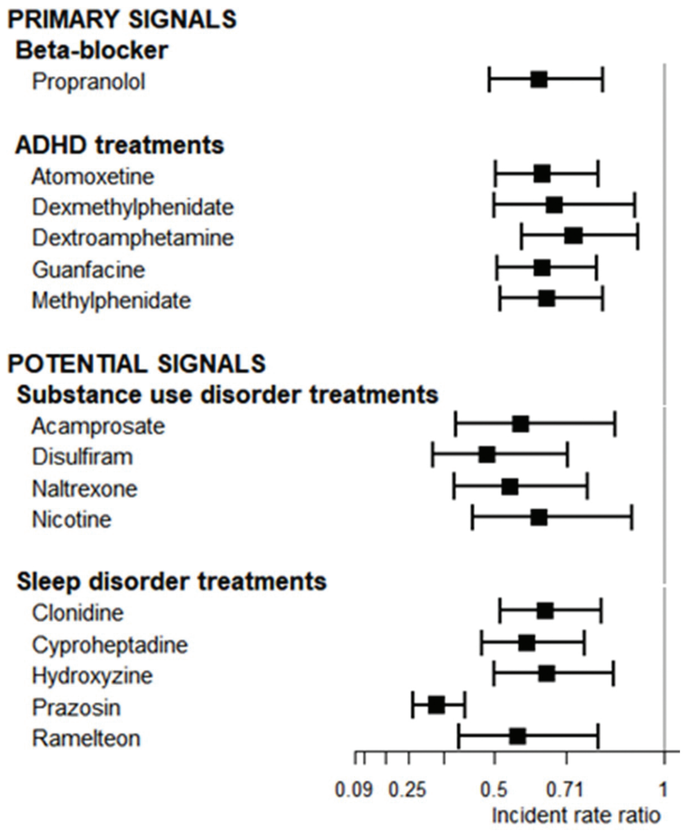
Disease incidence associations of a beta-blocker and medications used for ADHD, sleep disorders and substance use disorders recommend novel drug targets in the treatment of PTSD

RESULTS

Figure 2. Forest plots of meta-analyses of calibrated results for the medications found to have protective associations with PTSD



137,182,179 individuals were included in the analysis. Fifteen medications met the signal criteria and were classified as "primary signals" (those that have been previously investigated or proposed as potential therapies for PTSD) or "potential signals" (those whose effects may be confounded due to off-label use or the treatment of PTSD symptoms). This approach provides tangible targets for further research that can aid in the discovery of new and effective treatments for PTSD.

ADDITIONAL DATA

Medication	N exposed	Cases in exposed period	Cases in unexposed period	IRR	Lower 95%	Upper 95%
PRIMARY SIGNALS						
Beta-blocker						
Propranolol	992,417	2,763	4,678	0.63	0.49	0.82
ADHD treatments						
Atomoxetine	445,868	1,281	2,186	0.64	0.51	0.81
Dexmethylphenidate	374,128	776	1,169	0.68	0.50	0.91
Dextroamphetamine	1,465,446	3,964	5,847	0.73	0.58	0.92
Guanfacine	372,870	2,394	4,081	0.64	0.51	0.80
Methylphenidate	1,253,423	2,841	4,740	0.65	0.52	0.82
POTENTIAL SIGNALS						
Substance use disorder treatments						
Acamprosate	65,914	294	559	0.57	0.39	0.85
Disulfiram	51,818	189	406	0.48	0.32	0.72
Naltrexone	228,930	1,348	2,609	0.55	0.39	0.77
Nicotine	439,998	1,015	1,589	0.63	0.44	0.90
Sleep disorder treatments						
Clonidine	181,407	1,196	2,541	0.65	0.52	0.81
Cyproheptadine	434,670	480	878	0.60	0.47	0.76
Hydroxyzine	4,970,889	7,631	13,381	0.65	0.50	0.85
Prazosin	145,583	4,213	13,936	0.33	0.26	0.42
Ramelteon	185,246	257	481	0.57	0.40	0.81

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