RETROSPECTIVE ANALYSIS TO DETERMINE THE INCREASED RISK OF DEVELOPING OSTEOPOROSIS WITH DEPRESSION AND ANTIDEPRESSANT DRUGS.

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INTRODUCTION

Osteoporosis is a major health condition with significant morbidity and mortality. According to the National Osteoporosis foundation, approximately ten million Americans have osteoporosis. [1]. For the development of osteoporosis there are many risk factors which include increasing age, female sex, alcohol use, osteopenia, smoking, thin frame, inactivity and other medical conditions. Growing evidence shows that depression is another risk factor in developing osteoporosis as well, as shown in fig 1,2 [2].

According to the National Institute of Mental Health (NIMH) about 17.3 million US adults in 2017 had at least one major depressive episode. This represents about 7.1% of the US adult population [3]. Women are likely to take more antidepressants than men in every age group and it increases with older age [4]. Several studies have shown that the use of antidepressants, especially Selective Serotonin Reuptake Inhibitors (SSRI) and Tricyclic antidepressants (TCA) can develop into osteoporosis [5, 6,7]. To our knowledge there is no study comparing the effects antidepressant type (SSRI, TCA, SNRIs & MAO) and the subsequent development of osteoporosis.

METHODS

- **Using US medical and prescription claims data (2015 Q4 to 2019 Q3) female patients (F) between ages 55 to 85 years [median age 66 years] and male patients (M) between ages 65 to 85 years [median age 67 years] were studied retrospectively to analyze the effects of depression and antidepressant drugs on developing osteoporosis.**
- **They were classified into the following cohorts for both genders (C)- C1: Depression with antidepressants- Selective serotonin reuptake inhibitors (SSRIs) or Tricyclic antidepressants (TCAs), C2: Depression with antidepressants- Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) or Monoamine oxidase inhibitors (MAOIs), C3: Only depression (no antidepressants), C4: No depression and not on antidepressants as shown in table -1.**
- **Using waterfall criteria and applying all the inclusion and exclusion criteria we identified patients developing osteoporosis in each cohort.**

RESULTS

- **We observed an increased risk of osteoporosis in patients diagnosed with depression and not prescribed anti-depressants among both genders [C3 vs C4 - Odds ratio-OR (F)- 1.370254, OR (M)- 1.81021, $p < 0.001$].**
- **We also identified a further increased risk of osteoporosis with those receiving anti-depressants and some variation in specific antidepressant categories between genders.**
- **Female patients prescribed [SSRI ($p = 0.00261$) or TCA ($p < 0.0017$) or SNRI ($p = 0.0082$) or TCA and SSRI ($p < 0.001$)] had increased incidence of osteoporosis versus C3 or C4. Occurrence of osteoporosis in patients prescribed TCA was higher compared to SSRI. A logistic regression model was used to compute the odds ratios of developing osteoporosis for median age patients of different groups (TCA vs C3 - OR - 1.191, SSRI vs C3 – OR – 1.071).**
- **Male patients prescribed SNRI's (OR- 1.295335, $p < 0.001$) showed a significant risk in developing osteoporosis compared to other groups of antidepressants and untreated/controls. Below tables 2 and 3 shows the comparative statistical analyses between cohorts and individual group of drugs for both F and M.**

CONCLUSION

Incidence of osteoporosis was higher in older adults diagnosed with depression and increased further with antidepressants compared to only depression/no depression and patients not on antidepressants. We recommend adjusting current screening guidelines to reflect this increased risk. We also recommend consideration for more frequent monitoring and greater diligence to screening for osteoporosis in this vulnerable patient population.

Figure-1 ,2 Pathway linking depression developing osteoporosis

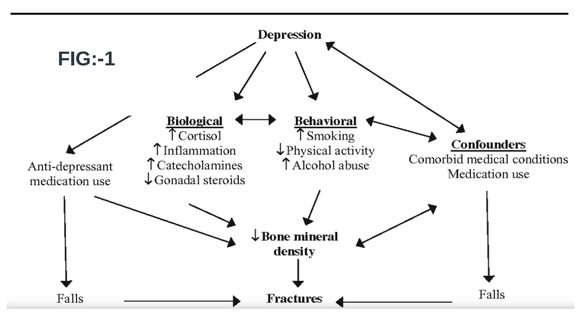


Fig. 1 Pathways linking depression, low bone mineral density, and fracture

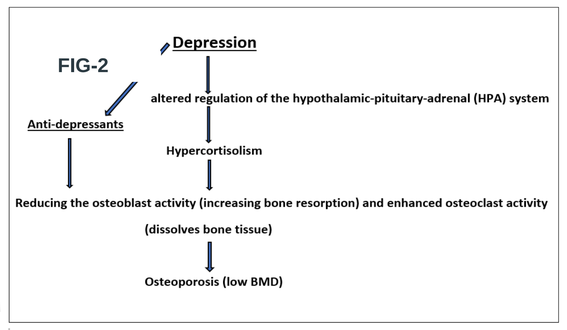
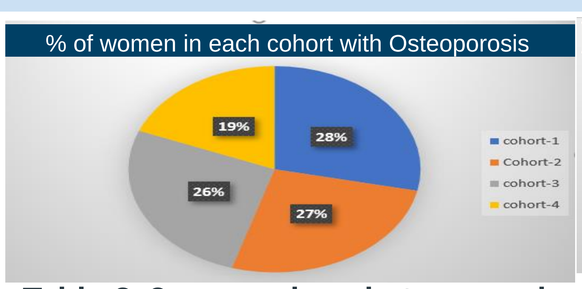


Table-1 Classification of Cohorts

Cohort-1 Depression and on antidepressants (SSRI or TCA)	Cohort-2 Depression and on antidepressants (SNRIs or MAO)
INCLUSION ❑Depression-patient diagnosis during 201810 – 201909, and lookback 3 years (201510-201809) from the most recent diagnosis to find if patients have at least 1 record claim during lookback 3 years ❑Age 55-85 years female , 65-85 Male ❑TCA or SSRI group of drugs during 201510- 201909 ❑Osteoporosis diagnosis during 201810 – 201909 **EXCLUSION** ❑MAO and SNRIs ❑corticosteroids >5mg – equivalent drugs for >3 months during 201510- 201909 ❑Osteoporosis -201510-201809	**INCLUSION** ❑Depression-patient diagnosis during 201810 – 201909, and lookback 3 years (201510-201809) from the most recent diagnosis to find if patients have at least 1 record claim during lookback 3 years ❑MAO or SNRIs group *of* drug during 201510- 201909 ❑Osteoporosis diagnosis during 201810 – 201909 **EXCLUSION** ❑TCA or SSRI and ❑corticosteroids >5mg- equivalent drugs for > 3 months during 201510- 201909 ❑Osteoporosis -201510-201809
Cohort-3 Depression and not on antidepressants	**Cohort-4 No depression and antidepressants**
INCLUSION ❑Depression-patient diagnosis during 201810 – 201909, and lookback 3 years (201510-201809) from the most recent diagnosis to find if patients have at least 1 record claim during lookback 3 years. ❑Age 55-85 years female , 65-85 Male ❑Osteoporosis diagnosis during 201810 – 201909 **EXCLUSION** ❑MAO and SNRIs and TCA or SSR and ❑corticosteroids >5mg- equivalent drugs for >3 months during 201510- 201909 ❑Osteoporosis -201510-201809	**INCLUSION** ❑Acute Nasopharyngitis-during 201810 – 201909, ❑Age 55-85 years female , 65-85 Male ❑Osteoporosis diagnosis during 201810 – 201909 **EXCLUSION** ❑Depression and Exclusion of TCA or SSRI or MAO, or SNRIs group of drugs and ❑corticosteroids >5mg- equivalent drugs for >3 months during 201510- 201909 ❑Osteoporosis -201510-201809



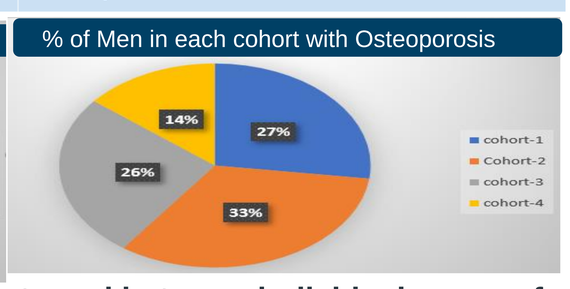


Table-2, 3 comparison between cohorts and between individual group of drugs in both Women and Men

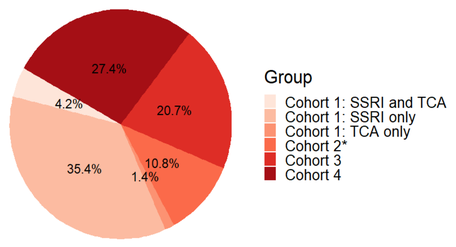
Table -2

	DESCRIPTION	ODDS RATIO	P-VALUE
Women	Depression vs no depression	1.370254	< 0.001
	Cohort 2 vs Cohort 3	1.073102	0.00629
	Cohort 1 vs Cohort 3	1.080158	< 0.001
Men	Depression vs no depression	1.81021	< 0.001
	Cohort 2 vs Cohort 3	1.296396	0.00166
	Cohort 1 vs Cohort 3		Not Significant

Table -3

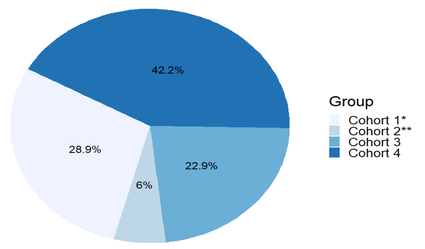
	DESCRIPTION	ODDS RATIO	P-VALUE
Women	SSRI and TCA vs Cohort 3	1.243617	< 0.001
	SSRI only vs Cohort 3	1.058005	0.00261
	TCA only vs Cohort 3	1.190888	0.00179
	SNRI only vs Cohort 3	1.070848	0.00819
	SNRI and MOA vs Cohort 3		Not Significant
	MOA only vs Cohort 3		Not Significant
Men	SSRI and TCA vs Cohort 3	1.243617	< 0.001
	SSRI only vs Cohort 3	1.058005	0.00261
	TCA only vs Cohort 3	1.190888	0.00179
	SNRI only vs Cohort 3	1.070848	0.00819
	SNRI and MOA vs Cohort 3		Not Significant
	MOA only vs Cohort 3		Not Significant

Women (1,829,663 patients)

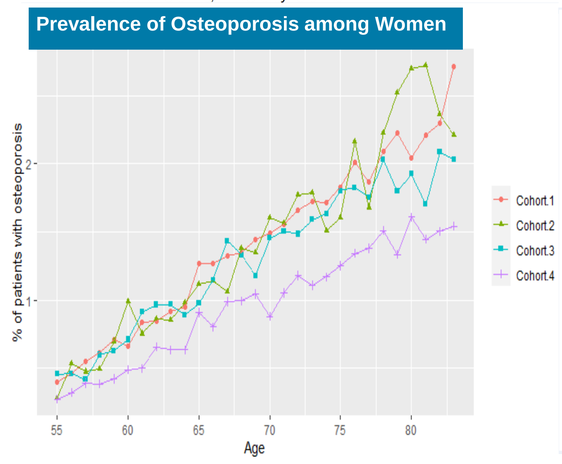


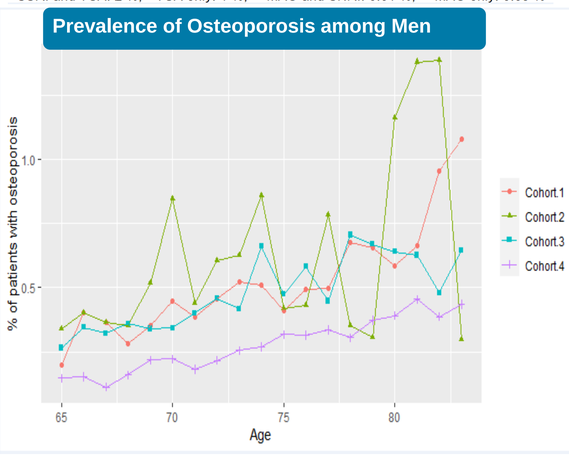
*MAO and SNRI: 0.01 %, MAO only: 0.04 %

Men (589,952 patients)



*SSRI and TCA: 2 %, *TCA only: 1 %, **MAO and SNRI: 0.01 %, **MAO only: 0.05 %





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