

THE COSTS ASSOCIATED WITH ANTIDEPRESSANT USE IN DEPRESSION AND ANXIETY IN COMMUNITY LIVING OLDER ADULTS

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BACKGROUND

- Antidepressants are among the most commonly used psychotropic drugs (Alexopoulos, 2005).
- Although antidepressants have met efficacy criteria in published clinical trials, meta-analyses including unpublished data have cast doubt on their effectiveness in real world settings (Christom, 2010; Kirsh, 2008; Pan, 2011).
- Because depression and anxiety may not be validly measured in administrative databases, a number of epidemiological and cost studies use therapy adherence or persistence rate as measures of effectiveness (Ereshefsky, 2010; Moride, 2002; Ron Cantrell, 2006; Sheehan, 2005; Tournier, 2009).
- To date, little is known about the health care costs associated with the remission or persistence of symptoms of depression and anxiety in antidepressant users in “real world” settings, in the older adult population.

OBJECTIVES

In a large representative community-dwelling older adult cohort population, the aim of this study is to assess:

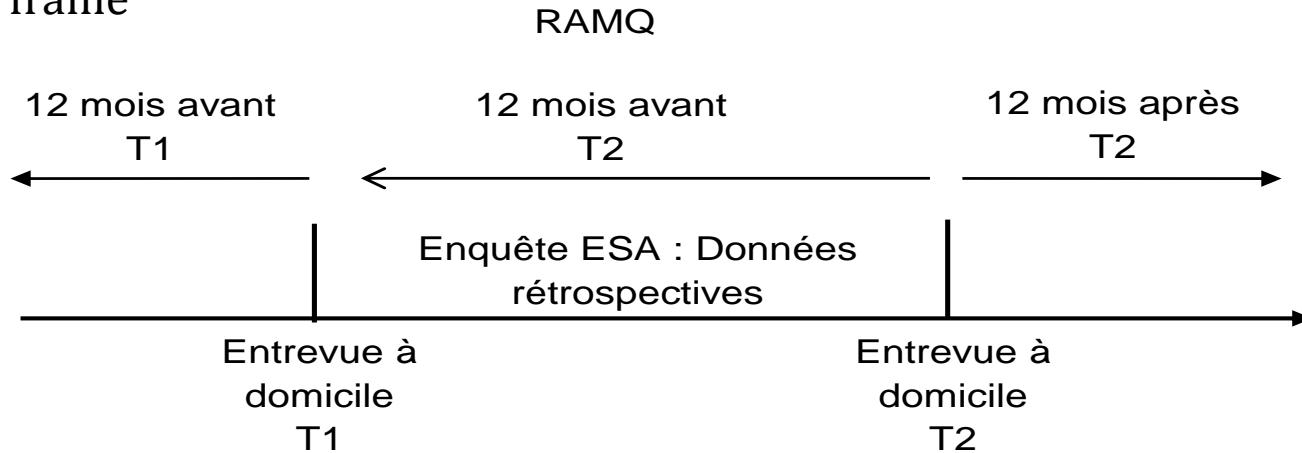
- The health care and patient costs associated with antidepressant use
- As a function of mental health status: change in status regarding the presence of depression and anxiety measured at two time points, one year apart

METHODS

Study sample

- This study was based on data collected in the **ESA Survey** (*Enquête sur la Santé des Aînés*- Survey on the Health of the Elderly) (n=2,811)
- Representative sample of community-dwelling older adults (>65y)
- Longitudinal retrospective study on the physical and mental health as well as health service use in the older adult population
- Participants completing both interviews and for whom access to RAMQ (Quebec's health insurance plan) data on medical services received and pharmaceutical data were included in the study (n=2,004) .
- The response rates at baseline and at the 12-month follow-up interview were 76.5% and 79.1%.

ESA time frame



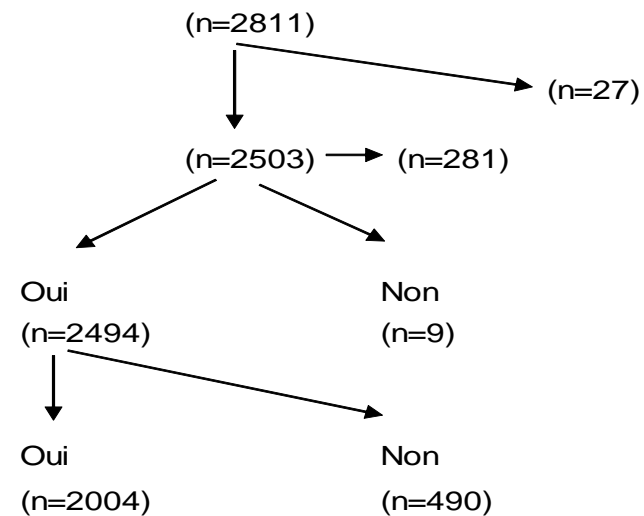
Échantillon initial de l'enquête ESA

Exclusion sur la base du statut cognitif (MMSE < 22)

Participants avec consentement valide et ayant donné l'accès à leur dossier RAMQ

Participants avec données de l'enquête ESA appariées aux données administratives de la RAMQ à T1

Participants ayant pris part aux deux entrevues de l'enquête ESA



METHODS

Measures

- Past year mental health status was measured, at baseline and at 12 months follow-up, using a computer-assisted questionnaire, the ESA Diagnostic Questionnaire (ESA-Q), based on DSM-IV criteria:
 - depression (major depression and minor depression)
 - anxiety (specific phobia, social phobia, agoraphobia, panic disorder, obsessive-compulsive disorder and generalized anxiety disorder).
- Respondents were categorized:
 - No depression/ anxiety
 - Persistent
 - Remission
 - Incident

METHODS

Measures

- Antidepressant use was identified from the RAMQ pharmaceutical services registry which includes, for residents with public drug insurance:
 - Each drug dispensed (DIN), the quantity, dosage, the date the prescription was filled, and the length of treatment, cost.
- Antidepressant use was considered for medications dispensed within three 6-month periods:
 - 6 month period prior to baseline interview
 - 6 month period following the baseline interview
 - 6 month period preceding the follow-up interview

METHODS

Cost data

- The cost analysis in this study was carried out from both the healthcare system and patient perspectives.
- Health service use was identified from the RAMQ and MED-ECHO databases.
- **Total healthcare costs** included the following: inpatient stays, emergency department (ED) and outpatient visits, physician fees and medications.
 - A hospitalization was valued on the basis of a cost per day .
 - ED and outpatient visits were valued as a cost per visit.
- **Patient costs included** : drug co-payments and those for transportation and the time spent by patients while seeking medical care.
 - Drug co-payments were obtained from the RAMQ pharmaceutical database.
 - Distance travelled for medical care was valued based on CRA vehicle rates for travel expenses
 - For outpatient and inpatient visits, an average time of 2 hours and 1 working day. The time spent was valued based on data reported by Statistics Canada estimating the replacement value of voluntary work.

ANALYSES

- Costs associated with AD use were studied as a function of mental health status at baseline and follow-up interviews: (i) no depression or anxiety at either interview; (ii) persistent: presence of either depression or anxiety at both interviews; (iii) remission and (iv) incident: presence of either depression or anxiety at either the baseline or follow-up interview.
- Generalized linear models with a gamma distribution (log link) were used to control for potential confounders.

ANALYSES

- Study variables controlled for:
 - age
 - sex
 - education (primary, secondary, post-secondary),
 - marital status (married vs separated/divorced/widowed/never married),
 - income (less than \$15,000 and \$15,000 and over),
 - region of residence (rural versus suburban, metropolitan),
 - number of chronic conditions (0-2 and 3+),
 - adherence to antidepressants measured by the medication possession ratio (MPR) for the 6 months prior to and following the baseline interview and 6 months preceding the follow-up interview.
 - The MPR represents the ratio between the number of days an antidepressant was supplied and the number of days corresponding to the follow-up period. Many have defined a good 6-month adherence measure as $\geq 80\%$.

RESULTS

Table 1. Relationship between socio-demographic, clinical factors and antidepressant use by depression and anxiety status (n=2004) ^{a,b}

| | Participants with depression ^c N (%)= 192 (9.6%) | | | | = | Participants with an anxiety disorder ^d N (%)=141 (7.1%) | | | | |
|------------------------|--|------------------------|------------------|--------------------|-------------------------------------|--|------------------------|------------------|--------------------|-------------------------------------|
| | No depression N=1812 | Incident cases N=67 | Remitted N=95 | Persistent N=29 | Wald χ^2 , df=3, p value | No anxiety N=1863 | Incident cases N=44 | Remitted N=69 | Persistent N=28 | Wald χ^2 , df=3, p value |
| 65-74 | 1043 (58%) | 41 (61%) | 61 (62.6%) | 21 (72.4%) | 4.25, p=0.13 | 1070 (57%) | 36 (83%) | 41 (60%) | 18 (64%) | 11.99, p=0.007 |
| 75 + | 769 (43%) | 27 (39%) | 34 (35.9%) | 8 (27.7) | | 793 (43%) | 7 (17%) | 28 (40%) | 10 (36%) | |
| Males | 785 (43%) | 21 (31%) | 26 (27.3%) | 12 (40%) | 13.47, p<0.01 | 809 (43%) | 9 (21%) | 15 (22%) | 10 (37%) | 21.10, p<0.001 |
| Females | 1027 (57%) | 47 (70%) | 69 (72.7%) | 17 (60%) | | 1054 (57%) | 35 (79%) | 53 (78%) | 18 (63%) | |
| < Post-Sec | 1169 (65%) | 50 (74%) | 61 (63.8%) | 23 (79%) | 5.09, p=0.17 | 1215 (65%) | 30 (67%) | 43 (62%) | 15 (52%) | 2.44, p=0.49 |
| Secondary | 643 (36%) | 18 (26%) | 35 (36.2%) | 6 (21%) | | 648 (35%) | 14 (33%) | 26 (38%) | 13 (48%) | |
| < \$15K/year | 404 (22%) | 24 (35%) | 24 (25.4%) | 9 (31%) | 7.42, p=0.06 | 415 (22%) | 14 (31%) | 27 (39%) | 6 (21%) | 11.78, p=0.008 |
| \$15K/year + | 1408 (78%) | 44 (65%) | 71 (74.6%) | 20 (69%) | | 1448 (78%) | 30 (69%) | 42 (61%) | 22 (79%) | |
| Married | 853 (47%) | 36 (54%) | 45 (47%) | 7 (24%) | 7.55, p=0.06 | 882 (47%) | 16 (37%) | 31 (45%) | 13 (46%) | 1.89, p=0.59 |
| Single/Wid | 959 (53%) | 31 (46%) | 50 (53%) | 22 (76%) | | 981 (53%) | 27 (63%) | 38 (55%) | 15 (54%) | |
| Sub./Metro | 1120 (62%) | 34 (50%) | 47 (49%) | 19 (64%) | 9.64, p=0.02 | 1135 (61%) | 23 (52%) | 45 (65%) | 17 (59%) | 2.08, p=0.55 |
| Rural | 692 (38%) | 33 (50%) | 49 (51%) | 11 (36%) | | 728 (39%) | 21 (48%) | 24 (35%) | 11 (41%) | |
| # of CC | | | | | 14.45, p=0.002 | | | | | 11.46, p=0.01 |
| 0-2 | 780 (43%) | 18 (26%) | 36 (38%) | 6 (19%) | | 796 (43%) | 14 (31%) | 17 (25%) | 14 (48%) | |
| 3+ | 1032 (57%) | 50 (74%) | 59 (62%) | 24 (81%) | 1067 (57%) | 30 (69%) | 52 (75%) | 15 (52%) | | |
| AD use | | | | | 67.53, p<0.01 | | | | | 42.35, p<0.001 |
| Yes | 262 (14%) | 20 (29%) | 35 (37%) | 14 (51%) | | 287 (15%) | 21 (48%) | 14 (20%) | 10 (36%) | |
| No | 1550 (86%) | 48 (71%) | 60 (63%) | 15 (49%) | 1576 (85%) | 23 (52%) | 55 (80%) | 18 (64%) | | |

a. All estimates are weighted. b. Differences of proportions based on χ^2 statistics. c. Depression included: major depressive disorder N=45 (2.2%); minor depressive disorder N=80 (4.0%). d. Anxiety disorder included: generalized anxiety disorder N=28 (1.4%); panic disorder N=14 (0.7%); specific phobia N=44 (2.2%); social phobia N=2 (0.1%); agoraphobia N= 4 (0.2%); obsessive-compulsive disorder N=27 (1.3%).

Table 2. Patterns of antidepressant use by depression and anxiety status

| | Among antidepressant users (n=332) | | | | | | | | | |
|-------------------|------------------------------------|------------------------|----------------------|--------------------------|---------|---------------------|------------------------|----------------------|--------------------------|---------|
| | Depression status | | | | | Anxiety status | | | | |
| | No depression N=262 | Incident cases N=20 | In remission N=35 | Persistent cases N=15 | p value | No anxiety N=287 | Incident cases N=21 | In remission N=14 | Persistent cases N=10 | p value |
| AD use | | | | | | | | | | |
| 6 months prior T1 | 210 (80%) | 10 (51%) | 26 (73%) | 10 (65%) | p=0.02 | 226 (79%) | 10 (46%) | 11 (81%) | 9 (90%) | p<.01 |
| 6 months post T1 | 219 (84%) | 16 (80%) | 29 (81%) | 5 (32%) | P<0.001 | 236 (82%) | 12 (56%) | 11 (81%) | 8 (80%) | p=0.05 |
| 6 months prior T2 | 226 (86%) | 16 (81%) | 31 (88%) | 9 (60%) | p=0.04 | 240 (84%) | 21 (100%) | 12 (84%) | 9 (88%) | p=0.98 |
| MPR ≥80% | | | | | | | | | | |
| 6 months prior T1 | 161 (61%) | 8 (41%) | 19 (54%) | 4 (26%) | p=0.02 | 168 (59%) | 7 (35%) | 9 (62%) | 8 (76%) | p=0.11 |
| 6 months post T1 | 157 (60%) | 8 (41%) | 22 (61%) | 5 (32%) | p=0.07 | 169 (59%) | 6 (28%) | 8 (59%) | 8 (76%) | p=0.03 |
| 6 months prior T2 | 166 (63%) | 12 (59%) | 24 (67%) | 6 (42%) | p=0.37 | 180 (63%) | 10 (47%) | 9 (64%) | 9 (88%) | p=0.16 |

T1: date of interview at baseline; T2: interview at one year follow-up

Table 3. Breakdown of costs by antidepressant use ^{a,b,c,d,e}

| | Government-borne health care costs | Patient costs | Total costs |
|------------------------|------------------------------------|---------------------------------|---------------------------------|
| | Mean (95% CI) | | |
| AD use (Yes/No) | Unadjusted estimates | | |
| Yes (N=332) | \$5845 (\$4813, \$6876) | \$1029 (\$811, \$1248) | \$6874 (\$5635, \$8113) |
| No (N=1672) | \$3464 (\$3112, \$3815) | \$579 (\$508, \$651) | \$4043 (\$3623, \$4463) |
| | $\chi^2= 18.34, df=1, p<0.0001$ | $\chi^2=14.70 df=1, p<0.0001$ | $\chi^2= 17.99, df=1, p<0.0001$ |
| | Adjusted estimates ^c | | |
| Yes (N=332) | \$5670 (\$4567, \$7039) | \$1191 (\$962, \$1474) | \$6861 (\$5586, \$8426) |
| No (N=1672) | \$3873 (\$3019, \$4968) | \$789 (\$617, \$1009) | \$4662 (\$3679, \$5908) |
| | $\chi^2=11.37, df=1, p=0.0007$ | $\chi^2= 13.46, df=1, p=0.0002$ | $\chi^2=12.88, df=1, p=0.0003$ |

a. All estimates are weighted. b.Wald Chi Square p-values with df=1 obtained from the generalized linear model with gamma distribution and log link. c. The dependent cost variables in the analyses were transformed as log (cost + 1). d. Cost estimates from gamma distribution, adjusted for: age, gender, education, revenue, marital status, rural region, number of chronic conditions, depression and anxiety status, and medication possession ratio ($\geq 80\%$) in the 6 months prior and post to baseline interview and 6 months prior to follow-up interview. e. Goodness of fit statistics for adjusted cost models: Scaled deviance was 1.25, 1.24, 1.23, and Scaled Pearson χ^2 was 1.61, 2.22 and 1.81, respectively.

Table 4. Adjusted total costs associated with level of antidepressant observance by depression and anxiety status^{a,b,c,d,e}

| | Adjusted total cost estimates, Mean (95% CI) | | | |
|-----------|--|--------------------------------|---------------------------------|--------------------------------|
| | Depression Status | | | |
| | No depression N=1812 | Incident cases N=68 | In remission N=95 | Persistent cases N=29 |
| No AD use | \$3489 (\$2738, \$4448) | \$6489 (\$2717, \$15 495) | \$4362 (\$2397, \$7935) | \$2205 (\$805, \$6038) |
| Use of AD | \$5479 (\$4440, \$6760) | \$14 533 (\$6869, \$30 749) | \$4285 (\$2497, \$7352) | \$1620 (\$813, \$3225) |
| | $\chi^2=13.20, df=1,$ p=0.0003 | $\chi^2=3.22, df=1,$ p=0.07 | $\chi^2=0.001, df=1,$ p=0.95 | $\chi^2=0.46, df=1,$ p=0.50 |
| | Anxiety Status | | | |
| | No anxiety N=1863 | Incident cases N=44 | In remission N=69 | Persistent cases N=28 |
| No AD use | \$4110 (\$3369, \$5168) | \$2009 (\$1181, \$3420) | \$4222 (\$2078, \$8576) | \$12584 (\$4976, \$31 821) |
| Use of AD | \$6102 (\$5037, \$7390) | \$3913 (\$2214, \$6913) | \$6556 (\$3597, \$11 951) | \$5993 (\$1807, \$19 871) |
| | $\chi^2=11.35, df=1,$ p=0.0008 | $\chi^2=4.42, df=1,$ p=0.04 | $\chi^2=0.89, df=1,$ p=0.35 | $\chi^2=0.79, df=1,$ p=0.38 |

a. All estimates are weighted b. Wald Chi Square p-values with df=1 obtained from the generalized linear model with gamma distribution and log link. c. The dependent cost variables in the analyses were transformed as log (cost + 1).

d. .Cost estimates from gamma distribution, adjusted for: age, gender, education, revenue, marital status, rural region, number of chronic conditions, depression and anxiety status, and medication possession ratio ($\geq 80\%$) in the 6 months prior and post to baseline interview and 6 months prior to follow-up interview.

DISCUSSION / CONCLUSION

- The overall annual prevalence of antidepressant use in this older adult population reached 16.6%.
- 36.1% and 31.9% of respondents with depression and anxiety, at either interview were dispensed an antidepressant.
 - In Europe, the ESEMeD (European study of the epidemiology of mental disorders) study reported overall past year prevalence rates of antidepressant use reaching 34.4%.
 - In the US, the rate of antidepressant use among older adults with depression in the past year has been reported as even higher, with levels of 63.1% in 2000 and 56.7% in 2004.
- We also observed that 15% of respondents not meeting DSM-IV criteria for depression and anxiety in the past year were also dispensed an antidepressant.
 - This represents 80% of respondents among antidepressant users. Beck et al (2005) also showed similar results where 60% of antidepressant adult users did not fill criteria for past year depression, but the majority had reported a lifetime presence of depression and anxiety.

DISCUSSION / CONCLUSION

- Respondents with persistent depression were less likely to be adherent in all three 6-month periods vs no depression and in remission.
- Overall, AD use was associated with increased total adjusted costs \$6861 (95% CI: \$5586, \$8426) vs \$4662 (\$3679, \$5908).
- AD use was associated with increased total adjusted costs in respondents with no depression and anxiety, and in respondents with incident anxiety.
 - Inpatient costs were significantly higher in antidepressant users with no depression
 - Antidepressant use was also associated with increased outpatient visits in people not reporting depression or anxiety
- Overall, the results did not show important cost savings or lower health service use associated with AD and this for all depression and anxiety groups.

STRENGTHS

- Unique data set, linking data from standardized questionnaires with extensive administrative data on health service use and costs.
- Depression and anxiety status is much more reliable than from billing data alone.
- The administration of standardized epidemiological questionnaires at two time points, one year apart, further refines the categorization of individuals by diagnostic status.
- The questionnaires permitted the assessment of physical health and the presence of co-morbidities for which we controlled.
- Fairly large sample selected at random, with a high response rate (above 75%) and a modest loss to follow-up (less than 20%).

LIMITATIONS

- The ESA study excluded people living in the northern regions, residing in institutions and the homeless. The conclusions of this study may therefore not apply to these groups, who usually exhibit different and more complex mental health problems and health service use.
- We did not assess the inter-rater reliability of the ESA questionnaires. However, interviewers were health professionals trained in interviewing techniques, and used highly standardized procedures in order to minimise the potential for such biases.
- The loss to follow-up was not at random. Non-participants at T2 were more likely to report a lower income and more likely to report a higher number of chronic conditions. They were not however more or less likely to report depression or anxiety during the first interview.

FUTURE RESEARCH

Future studies should focus on:

- Exploring the potential cost savings, if any, associated with different classes of antidepressants in the treatment of depression and anxiety and this in the older adult population,
- Exploring the potential for reducing costs in those discontinuing use of antidepressants once depression has remitted.
- Assess longer follow-up period: prior episodes of depression/anxiety and AD use
- Replicating this in the adult population: examine whether indirect costs associated with loss in productivity will impact the results
- Include health related quality of life measures

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