Analysis of Anticholinergic Medication Effect on Cognitive and Functional Decline Among Older Adults

Etwal Bou Raad, PharmD, MPH, PhDc

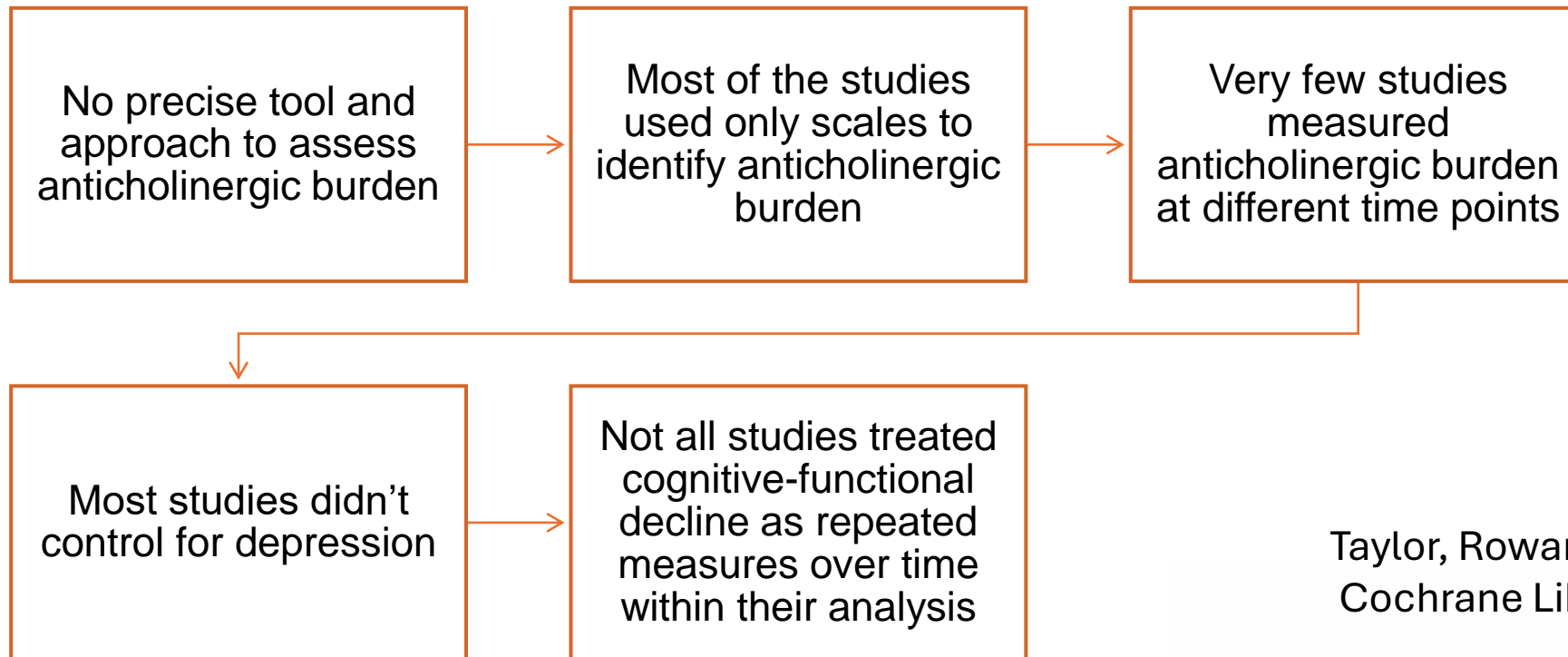*American University of Beirut, Lebanon*

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Analysis of Anticholinergic Medication Effect on Cognitive and Functional Decline Among Older Adults

No precise tool and approach to assess anticholinergic burden

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Most of the studies used only scales to identify anticholinergic burden

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Very few studies measured anticholinergic burden at different time points

Most studies didn't control for depression

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Not all studies treated cognitive-functional decline as repeated measures over time within their analysis

Taylor, Rowan, 2021
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Analysis of Anticholinergic Medication Effect on Cognitive and Functional Decline Among Older Adults

Study Objectives:

- To validate an approach that can quantify the anticholinergic burden
- To evaluate the association between the use of anticholinergic burden and cognitive-functional decline among older adults using longitudinal analysis controlling for potential covariates

Anticholinergic Burden Scales

19 scales are available to identify medications with different anticholinergics properties

(Boustani, 2008)

Anticholinergic cognitive burden scale (ACB)

- Validated in a wide range of populations of older adults of different age-groups
- Achieved the highest percentage in rigorous of development, number of validation, applicability and clarity of presentation (Angela Lisbach, 2021)
- Includes 88 medications
- Mild (score=1), moderate (score=2) and severe (score=3)

Anticholinergic and Sedative Burden Catalog (ACSBC)

(Al Rihani, 2021)

- Combined 13 anticholinergic burden scales
- List of 642 anticholinergic drugs with related anticholinergic properties and their sedative effects
- None (score=0), low (score=1), moderate (score=2) and high (sore =3)

Anticholinergic Burden Measures
Average Daily Formula

- Originally developed by Campbell et.al using the ACB scale

- Ratio between the sum of the anticholinergic score for each anticholinergic medication taken by the patient multiplied each by the exposure time over the total follow up period

- Compared to the cumulative dose measure, it is considered practical approach to quantify anticholinergic burden

Campbell, 2016

$$\text{Mean total ACB score} = \frac{\sum (\text{Drug A \#days supplied} \times \text{ACB score}) + (\text{Drug B \#days supplied} \times \text{ACB score}) + (\text{Drug X}\ldots)}{\text{\#days from first prescription date to index date} \textbf{(date of cognitive screening)}}$$
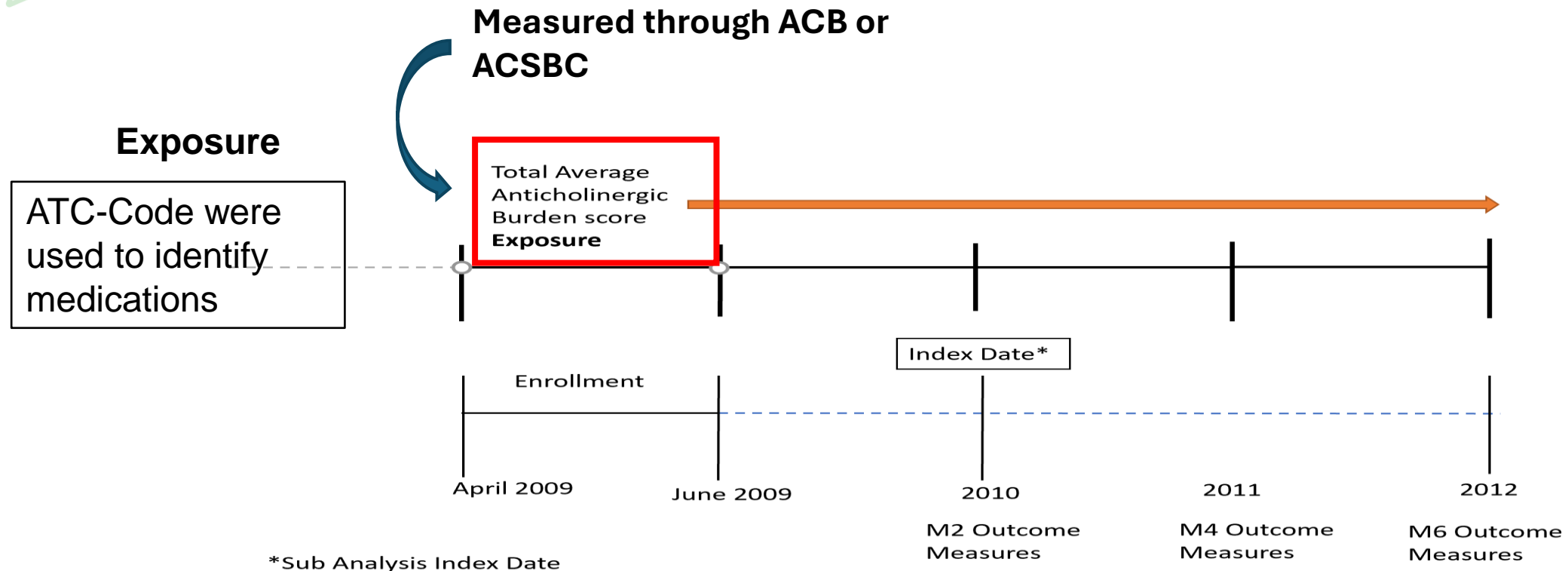
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Study Base : S.AGES 9 (Sujets Ages, elderly subjects) conducted in Metropolitan France from 2009 till 2012 among older adults Total of 983 patients were recruited through their general practitioner
(Becquemont L, 2013)

Measured through ACB or ACSBC

Exposure

ATC-Code were used to identify medications

Total Average Anticholinergic Burden score **Exposure**

Index Date*

Enrollment

April 2009   June 2009   2010   2011   2012

M2 Outcome Measures   M4 Outcome Measures   M6 Outcome Measures

*Sub Analysis Index Date

Mini-Mental State Examination (MMSE)
Basic activity of daily livings (Basic ADLs)
Instrumental of daily livings (IADLs)

Outcomes: MMSE and ADLs (Basic ADLs and IADLs)

Statistical Analysis Plan

Objectives	Analysis Plan
Estimate the average daily Anticholinergic burden using ACB and ACSBC	Average Daily Formula
Estimate the bivariate association between the study outcomes and covariates	Student T test, ANOVA, Post Hoc analysis
Missing Data	Maximum likelihood estimates to estimate the averages of our exposures and outcomes
Estimate the level of correlation between the total average anticholinergic burden scores	Spearman correlation
Compare the adjusted β estimates between the two anticholinergic burden scores and study outcomes	Linear mixed models (Xtmixed) Time dependent Variables: Age, visit and Daily total Anticholinergic Burden measured by the two scales Covariates: age, education, occupation, smoking, alcohol, living status, region, comorbidities, depression

Spearman correlation between the average daily ACB score and ACSBC

Visit	Mean (SD)		rho	P value
At baseline (Visit1) *			0.7567	**<0.001**
ACSBC	0.712(1.22)			
ACB scale	0.42 (0.96)			
After 12 months (Visit 2) ^			0.7118	**< 0.001**
ACSBC	0.67(1.09)			
ACB scale	0.39(0.85)			
After 24 months (Visit 4) ^			0.7194	**<0.001**
ACSBC	0.73 (1.03)			
ACB scale	0.41(0.80)			
After 36 months (Visit 6) ^			0.6978	**<0.001**
ACSBC	0.745 (0.94)			
ACB scale	0.42(0.75)			

Spearman correlation between the total daily ACB score and ACSBC at baseline and after 12 months (visit3), 24 months(visit5) and 36 months(visit7).

*Baseline anticholinergic burden was computed by summing individual anticholinergic medication estimated through ACB and ACSBC. Total daily anticholinergic burden at visit 1 is 0.
^ACB & ACSBC   total daily doses estimated by the total dose formula.

Variables	Model 1				Model 2				Model 3			
	MMSE	SE	P Value	95% CI	Basic ADLs	SE	P Value	95%CI	IADLs	SE	P Value	95%CI
ACB	-0.12	0.07	0.096	(-2.64, 0.02)	-0.02	0.013	**0.039**	(-0.05, -0.001)	-0.05	0.02	**0.013**	(-0.09, -0.01)
Visit	-0.22	0.02	**<0.0001**	(-0.26, -0.17)	-0.03	0.005	**<0.0001**	(-0.04, -0.02)	-0.04	0.006	**<0.0001**	(-0.06, -0.033)

Variables	Model 3				Model 4				Model 5			
	MMSE	SE	P Value	95% CI	Basic ADLs	SE	P Value	95%CI	IADLs	SE	P Value	95%CI
	β Coeff				β Coeff				β Coeff			
ACSBC	-0.03	0.07	0.586	(-0.18,0.10)	-0.032	0.013	**0.017**	(-0.059, -0.005)	-0.06	0.02	**0.002**	(-0.105, -0.02)
Visit	-0.22	0.02	**<0.0001**	(-0.26, -0.17)	-0.03	0.005	**<0.0001**	(-0.04, -0.02)	-0.04	0.006	**<0.0001**	(-0.06, -0.03)

Table 1 summarizes the association between the total daily ACB score and the total daily MMSE (Model1), ADLs (model 2) and IADLs (model 3) scores adjusted for the study covariates including the estimates, standard errors and P values. Only significant variables were kept in the final models.

Table 2 summarizes the association between the total daily ACSBC score and the total daily MMSE (Model4), ADLs (model 5) and IADLs (model 6) scores adjusted for the study covariates including the estimates, standard errors and P values. Only significant variables were kept in the final models.

Strengths & Limitations

Strengths	Limitations
Modeled average daily anticholinergic burden with cognitive and functional decline over the period of follow up	Longer period of follow up is needed to monitor cognitive and functional decline
Provides geriatricians and evidence based approach to measure total daily anticholinergic burden and helps in taking a decision for deascelation	Considered drug interaction as part of the anticholinergic burden score

In Summary

- Our findings supported the association between average daily anticholinergic burden and functional decline
- Evidence regarding the approach to measure anticholinergic burden is still warranted to generate a clear recommendations about anticholinergics and long term adverse effects
- Integrating the assessment of anticholinergic burden at point of care that promote deascelation is essential to heighten health care among elders and reduce cost of care