

# Chapter 24

## Costs factors in diagnosing dementia

*Serge Gauthier, Anders Wimo*

### Key points

- Adequate training of medical students and family practitioners is the most cost-effective approach for a timely and accurate diagnosis of dementia.
- Costs associated with a timely and accurate diagnosis are preferable to a delayed or inaccurate diagnosis that impedes a structured management of the condition.
- In relation to the emergence of biomarkers leading to an earlier and more specific diagnosis of dementia, further work is required to find cost-effective ways to orient people towards the best diagnostic pathways.



## General background

When the cost factors in diagnosing dementia were studied in 1998, the main finding was that the human element, meaning the clinician's time, was the most important component, yet the least expensive when compared to costs associated with blood tests and structural brain imaging (1). In 2014, Wimo et al (2) carried out a detailed cost analysis on the diagnosis of dementia, including a breakdown of each diagnostic procedure and anticipating

the proposed biological diagnosis of Alzheimer disease using the Amyloid, Tau, Neurodegeneration (ATN) framework (3).

Diagnostic costs have been studied in Sweden (4,5) and in Germany (6), highlighting the variability of costs based on the type of cognitive impairment and the setting (community setting versus a specialised clinic).

## Survey results

The 1,111 multidisciplinary clinicians who responded to this survey were from high income (62%) and low- and middle-income countries (38%) using the 2021 World Bank listings of countries as reference. Most were working under a public healthcare system (50%), a good many in a mixed public and private system (30%), and the minority in private only systems (20%). When questioned about whether costs were a limiting factor in using specific diagnostic tests if they were available in their country, the main obstacle reported was with amyloid PET imaging (32%), followed by FDG-PET (29%), CT/MRI (18%), genetic testing (17%), CSF

analysis for amyloid and tau proteins (14%). Costs were not a factor in referring a young person with dementia to a specialised clinic (2%), nor were they the primary issue in accepting to use novel blood biomarkers (14%) or in using remote cognitive testing (2%).

Among the 2,327 persons with dementia and their carers who replied to their survey, only 19% raised financial constraints as a major issue in getting a diagnosis, compared to lack of information provided about dementia (41%).

## Additional considerations

When preparing this World Alzheimer Report, an effort was made to document the current costs of a dementia diagnosis. Most of the clinicians who replied indicated that the costs were covered by their country or state public healthcare system and that they were unaware of the specific costs. Thus, a worldwide cost analysis is needed for diagnostic procedures associated with dementia. A template is proposed in Tables 1a and 1b using the Province of Quebec's current costs per medical visit for people over the age of 65 in an outpatient clinic setting within the public healthcare system, as well as laboratory procedures in the public healthcare system or in private facilities. Costs are in Canadian Dollars unless otherwise indicated. Further work is clearly necessary in order to promote cost effective ways that orient people concerned with cognitive decline towards the best diagnostic pathway.

Comparing diagnostic pathways using current costs in Quebec versus costs published in 2014 by Wimo et al., with Swedish cost data is pertinent (Table 2) (2). Of note, from a clinical perspective, the sequence of events would be PC, SCE, NP, MRI, then CSF or PET.

The current costs of diagnosing dementia for people over the age 65 is lowest when most of the diagnosis is handled by family practitioners and emphasis is placed on history, physical examination, basic cognitive testing, the minimal required laboratory tests to exclude common comorbidities, and one brain imaging study (CT or MRI, the latter being preferable). In Quebec, these costs would include two visits with a family practitioner, bloods and a CT (total \$198.30) or an MRI (\$484.30).

In people younger than 65, there is a broader differential diagnosis that usually requires a referral to a neurologist with additional expertise in early-onset dementias. There will be additional laboratory tests and likely a spinal fluid examination (see Chapter 23). In Quebec, these total costs include two visits to a family practitioner and a referral to a neurologist providing two visits, one MRI, one FDG-scan and either a spinal fluid study (total \$2,108.00) or a PET-amyloid scan (total \$4,503.00). Special blood tests on a case-by-case basis are not included.

If a biological diagnosis for the cause of the dementia is the result of Alzheimer's disease, access to new anti-amyloid therapies may be needed. Thus, specific biomarkers studies are required to confirm amyloid positivity, and there is a need to validate a cost-effective algorithm such as the one proposed in Table 3 using APOE genotyping (\$43) as a starting point. The high (95+) amyloid positivity in APOE4 4/4 has been reported by Degenhardt et al., 2016 (7). Elevated P-Tau 181 plasma levels are promising as surrogate to CSF analysis (8,9) and PET imaging (10), and the cost is expected to be less than CSF analysis. This algorithm may prove particularly useful when diagnosing people over the age of 70 (11).

Finally, if the person is clinically diagnosed as having mild cognitive impairment, the diagnostic approach will differ if there is a wait and see approach, taking advantage of secondary prevention through control of vascular risk factors and emphasis on health lifestyles (Diagnostic pathway 1 in Table 2), versus a disease-modifying drug requiring full clinical and etiologic work-up (Diagnostic pathways 13 and 15 in Table 2). As highlighted by Wimo et al in 2014, false positives and false negatives may have more consequences at that stage (2).

Current costs of dementia diagnosis related to visits (Table 1a) and procedures (Table 1b) in a hospital outpatient clinic, in the province of Quebec, Canada, under a universal publicly funded Medicare system.

**Table 1a. Assessments by physicians (First visit and one follow-up visit for persons over the age of 65)**

	First Visit	Follow-up Visit
Family practitioner	100.00	50.00
Neurologist	320.00	77.00
Psychiatrists	359.00	140.00
Geriatricians	350.00	250.00
Geneticists	323.00	105.00
	<b>PUBLIC</b>	<b>PRIVATE</b>
Assessments by other healthcare professionals		
Genetic counsellor	140.00	Not available
Neuropsychologist	500.00	2,300.00

**Table 1b. Laboratory tests**

	PUBLIC	PRIVATE
<b>Blood Tests</b>		
Complete Blood Count (CBC)	1.30	52.00
Sedimentation rate	1.60	39.00
Thyroid Stimulation Hormone (TSH)	1.60	89.00
T4	1.80	79.00
Electrolytes	2.10	69.00
Calcium	0.80	35.00
Blood Urea Nitrogen (BUN)	0.70	29.00
Creatinine	0.70	37.00
Glycemia	0.70	37.00
Haemoglobin A1c (HbA1c)	3.20	62.00
Alanine Aminotransferase (ALT)	0.70	31.00
B12	2.50	62.00
Folate	3.30	59.00
Cholesterol total, HDL, LDL, Triglycerides	5.30	79.00
Homocysteine	10.80	129.00
Syphilis serology	3.50	69.00
Human Immunodeficiency Virus (HIV) screen	4.90	69.00
<b>Electroencephalography (EEG)</b>		
Routine awake EEG	300.00	450.00
<b>Spinal Fluid</b>		
Lumbar puncture (procedure and kit)	205.00	205.00
Measure of A-Beta, Total tau and P-Tau	400.00	1349.00USD
<b>Brain imaging</b>		
Non contrast computer tomography (CT)	34.00	300.00
Non contrast magnetic resonance imaging (MRI)	320.00	650.00
Positron Emission Tomography (PET) with fluorodeoxyglucose (PET-FDG)	636.00	1,750.00
PET with amyloid ligand florbetaben	3,000.00	Not available
<b>Genetic Testing</b>		
APOE	43.00	219.00
PS1, PS2, APP	890.00 USD	890.00 USD

Prices are in Canadian Dollars unless otherwise indicated.

Table 2. Comparison of 2014 costs in Sweden to current costs in Quebec for different diagnostic pathways when Alzheimer's disease is suspected.

Diagnostic	Sequence of tests	Costs in 2014	Costs in 2021
Pathway		<i>in Sweden (US\$)</i>	<i>In Quebec (US\$)</i>
Dia 1	PC	860	160
Dia xvf2	PC+SCE	1330	481
Dia 3	PC+SCE+MRI	1700	740
Dia 4	PC+SCE+CSF	2130	970
Dia 5	PC+SCE+NP	1870	885
Dia 6	PC+SCE+PET	2760	2906
Dia 7	PC+SCE+MRI+CSF	2500	1229
Dia 8	PC+SCE+MRI+NP	2240	1144
Dia 9	PC+SCE+MRI+PET	3130	3165
Dia 10	PC+SCE+CSF+NP	2670	1375
Dia 11	PC+SCE+CSF+PET	3560	3395
Dia 12	PC+SCE+NP+PET	3300	3311
Dia 13	PC+SCE+MRI+CSF+NP	3040	1633
Dia 14	PC+SCE+MRI+CSF+PET	3930	3654
Dia 15	PC+SCE+MRI+NP+PET	3670	3569
Dia 16	PC+SCE+CSF+NP+PET	4100	3800
Dia 17	PC+SCE+MRI+CSF+NP+PET	4470	4058

*Dia*, diagnostic pathway; *PC*, primary care (includes two clinical examinations, basic laboratory tests, computed tomography scan); *SCE*, specialist two clinical examinations (neurologist rate for the 2021 data); *MRI*, magnetic resonance imaging; *CSF*, spinal tap, kit and cost of analysis; *NP*, neuropsychological examination; *PET*, positron emission tomography for amyloid.

### Table 3. Proposal to streamline the biological diagnosis of dementia due to Alzheimer's disease

- APOE 4/4 = A (+) very high (95%+) probability; no need for CSF or amyloid PET
- APOE 4/3 = A (+) moderate to high probability; requires plasma p-Tau 181 – if elevated, no need for CSF or PET
- APOE 4/3 with normal plasma p-Tau 181 or APOE3/3 = A (+) moderate probability, requires CSF or PET

## Conclusions

A timely and accurate diagnosis of dementia entails some costs, but they are offset by a delayed or inaccurate diagnosis that impedes a structured management of the condition.

Comparing global healthcare systems and developing optimal diagnostic pathways from a cost perspective is vital. That said, the approach must also account for a time-effective clinician approach that incorporates time to provide necessary information to people with cognitive decline and their families.

## Additional references

1. Gauthier S. Costs of diagnostic procedures. In: Wimo A, Jönsson B, Karlsson G, Winblad B, editors. *Health Economics of Dementia*. John Wiley & Sons Ltd; 1998. p. 269–73.
2. Wimo A, Ballard C, Brayne C, Gauthier S, Handels R, Jones RW, et al. Health economic evaluation of treatments for Alzheimer's disease: Impact of new diagnostic criteria. *J Intern Med* [Internet]. 2014 [cited 2021 Jul 12];275(3):304–16. <https://pubmed.ncbi.nlm.nih.gov/24605810/>
3. Jack CR, Bennett DA, Blennow K, Carrillo MC, Feldman HH, Frisoni GB, et al. A/T/N: An unbiased descriptive classification scheme for Alzheimer disease biomarkers. Vol. 87. *Neurology*. 2016. p. 539–47.
4. Wimo A, Religa D, Edlund AK, Winblad B, Eriksdotter M, Spångberg K. Costs of diagnosing dementia: Results from SveDem, the Swedish Dementia registry. *Int J Geriatr Psychiatry* [Internet]. 2013 Oct [cited 2021 Jul 12];28(10):1039–44. <https://pubmed.ncbi.nlm.nih.gov/23440702/>
5. Jedenius E, Wimo A, Strömqvist J, Jönsson L, Andreasen N. The cost of diagnosing dementia in a community setting. *Int J Geriatr Psychiatry* [Internet]. 2010 May [cited 2021 Jul 12];25(5):476–82. <https://pubmed.ncbi.nlm.nih.gov/19685441/>
6. Michalowsky B, Flessa S, Hertel J, Goetz O, Hoffmann W, Teipel S, et al. Cost of diagnosing dementia in a German memory clinic. *Alzheimer's Res Ther* [Internet]. 2017 Aug 22 [cited 2021 Jul 12];9(1). <https://pubmed.ncbi.nlm.nih.gov/28830516/>
7. Degenhardt EK, Witte MM, Case MG, Yu P, Henley DB, Hochstetler HM, et al. Flortetapir F18 PET Amyloid Neuroimaging and Characteristics in Patients With Mild and Moderate Alzheimer Dementia. *Psychosomatics*. 2016 Mar 1;57(2):208–16.
8. Alcolea D, Delaby C, Muñoz L, Torres S, Estellés T, Zhu N, et al. Use of plasma biomarkers for AT(N) classification of neurodegenerative dementias. *J Neurol Neurosurg Psychiatry* [Internet]. 2021 [cited 2021 Jul 12]; <https://pubmed.ncbi.nlm.nih.gov/34103344/>
9. Hansson O. Biomarkers for neurodegenerative diseases [Internet]. Vol. 27. *Nature Medicine*. Nature Publishing Group; 2021 [cited 2021 Jul 12]. p. 954–63. <https://www.nature.com/articles/s41591-021-01382-x>
10. Tissot C, Kunach P, Theriault J, Benedet A, Pascoal T, Ashton N, et al. Comparing tau status determined via plasma pTau181, pTau 231 and t18FIMK6240 PET. *Neurol* [Submitted]. 2021;
11. Ossenkoppele R, Jansen WJ, Rabinovici GD, Knol DL, van der Flier WM, van Berckel BNM, et al. Prevalence of amyloid PET positivity in dementia syndromes: a meta-analysis. *JAMA* [Internet]. 2015 May 19 [cited 2021 Jul 12];313(19):1939–49. <https://pubmed.ncbi.nlm.nih.gov/25988463/>