Cost-consequence analysis of dimethyl fumarate *versus* other disease-modifying therapies in Multiple Sclerosis: a French cohort study with SNDS national claims database in France

Pauline Bosco-Lévy[1,2], Patrick Blin[1], Séverine Lignot-Maleyran[1], Régis Lassalle[1], Abdelilah Abouelfath[1], Pauline Diez-Andreu[1], Marc Debouverie[3], Bruno Brochet[4], Francis Guillemin[5], Nicholas Moore[1,6], Cecile Droz-Perroteau[1]

[1] Bordeaux PharmacoEpi, Univ. Bordeaux-INSERM CIC1401, Bordeaux, France, [2] Bordeaux Population Health Research Centre, INSERM UMR 1219, Univ. Bordeaux, Bordeaux, France, [3] Département de neurologie, CHU Nancy, F-54035 Nancy, France ; Université de Lorraine, EA 4360 APEMAC, F 54500 Vandoeuvre-Lès Nancy, France, [4] CRC SEP, service de Neurologie, CHU de Bordeaux, [5] CHRU de Nancy, INSERM CIC 1433 Epidémiologie clinique, Nancy, Université de Lorraine, EA 4360 APEMAC, F 54500 Vandoeuvre-Lès Nancy, France, [6] CHU de Bordeaux, Bordeaux, France

Background

- **Multiple sclerosis (MS)**
  - Incapacitating, progressive, chronic neurological disorder that involves a selective, chronic inflammation and demyelination of the central nervous system
  - Relapsing-remitting MS form (RRMS) is the most common, and are characterized by the presence of relapses without disability progression between relapses
  - In France, prevalence in 2015: 135 per 100 000 inhabitants and 87 000 cases in 2017
- **Current therapeutic strategy of RRMS**
  - The first-line generation of medications approved were the Injectable ImmunoModulators (**IMM**)
  - Treatment options have broadened to include the orally administered: dimethylfumarate (**DMF**), teriflunomide (**TERI**) and fingolimod (**FTY**).
- The **cost-consequence** of DMF *versus* other first-line (IMM and TERI) or second-line (FTY) disease-modifying therapies **has never been studied** in real world settings using data of a **national claims database.**
- **In this context, a project was designed** to assess the **effectiveness and the cost-consequence** of DMF compared to IMM, TERI and FTY, in real life setting.

Objectives

- **To assess the cost-consequence of DMF versus other disease-modifying therapies indicated in multiple sclerosis (i.e. IMM and two other oral drugs: FTY and teriflunomide TERI) in real world settings using data of a national claims database**

Declaration of Interest Statement

This study is carried out by the Bordeaux PharmacoEpi platform in collaboration with Biogen. This work was supported by Biogen and supervised by an independent scientific committee

Methods

- **Study Design (figure 1)**

  Cohort study using SNDS (*Système National des Données de Santé*) nationwide French claims database including all patients with a first reimbursed dispensing of a MS drug from 2015 to 2017, a follow-up from 1 to 3.5 years after initiation (i.e. index date) and at least 4.5-year database history.

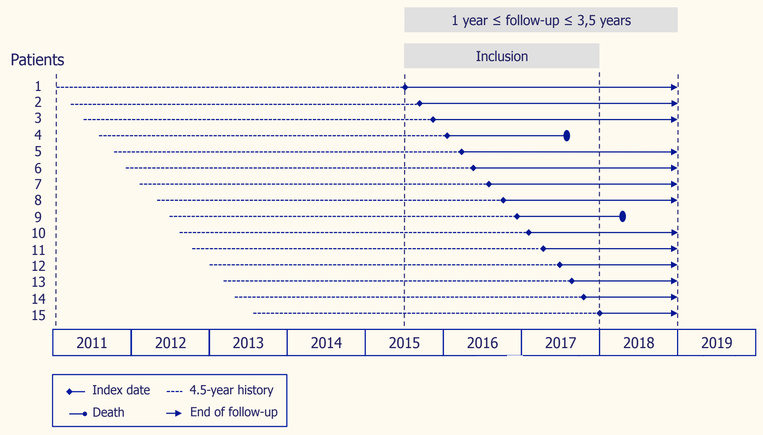

Figure 1. Study design

- **Data source**

The SNDS database contains individual pseudonymised information from 66 million persons on:

- Gender, date of birth, area of residence, date of death;
- Long-term disease registration with associated ICD-10 codes for full insurance coverage;
- Outpatient reimbursed healthcare expenditures: visits, medical procedures, lab tests, drugs …;
- Hospital discharge summaries with ICD-10 codes for diagnosis (primary, linked and associated diagnoses) for all private and public medical, obstetric and surgery hospitalisations, with the date and duration of hospitalisation, medical procedures.

- **Outcome**
  - The effectiveness was assessed in each treatment group by estimating the Annual Rate of Relapses (ARR), which were identified using a validated algorithm.
- **Costs**
  - The costs were estimated in euros according to the **collective perspective** during the first index treatment exposure period.
  - Healthcare resources taken into account for the description of the costs of treatment groups:
    - ✓ **Global healthcare resources** use according to the different areas of expenditure: drugs; medical consultations, visits and technical acts; nursing acts; physiotherapy acts; lab tests; products and services; transport; other medical healthcare resources; public hospital external consultations and acts (Medicine, Surgery and Obstetric: MCO); hospitalizations (MCO); sick leaves and daily allowances; assistance, pension and disability allowances; other non-medical healthcare resources;
    - ✓ **Specific healthcare resources** use according to the following specific areas of expenditure:
      - drugs used specifically in the treatment of MS;
      - MS specific hospitalisations, including related transport;
      - neurologist medical visits, including related transport;
      - MS specific lab tests, including related transport and related nursing acts plus majoration and travel allowances;
      - MS specific medical devices.
- **Data analyses**
  - DMF effectiveness was compared to other treatment groups during the index treatment period after trimming and matching on a high dimensionnal Propensity Score (hdPS) . Results were expressed in Relative Risk (RR).
  - Annual costs of all reimbursed healthcare expenditures were measured for DMF and the other treatment groups from the collective perspective, overall and by cost components (inpatient, medication and non-medication costs).

Results

- After hdPS matching and exclusion by trimming, **1679 patients DMF and TERI** were included, **1780 patients DMF and IMM**, and **376 patients DMF and FTY**.
- **Effectiveness**
  - **DMF proved to be significantly effective on ARR in comparison with IMM and TERI** (RR: 0.72 and 0.81, respectively). No significant difference was found with FTY, but patients characteristic remained unbalanced between both treatment groups even after hdPS matching.
- **Annual global cost (costs of all healthcare expenditures) in treatments groups (Figures 1, 2, 3)**
  - Mean overall cost per person-year for **DMF was significantly higher than for TERI** (14531€ (±8022) vs. 13197€ (±7848)) (*p<0.0001*), and IID (14273 € (±7992) vs. 12476€ (±7828)) (*p<0.0001*),
  - In comparison to FTY, **overall costs were significantly lower for DMF** (15575€ (±11668) vs. 24206€ (±13222)) (*p<0.0001*),
  - **Additional cost being mainly due to the medication costs** (10352€ (±4555) vs. 8640€ (±3526) and 10275€ (±4476) vs. 8130€ (±3638), respectively for each treatment group),

- **Annual global cost DMF *versus* TERI**

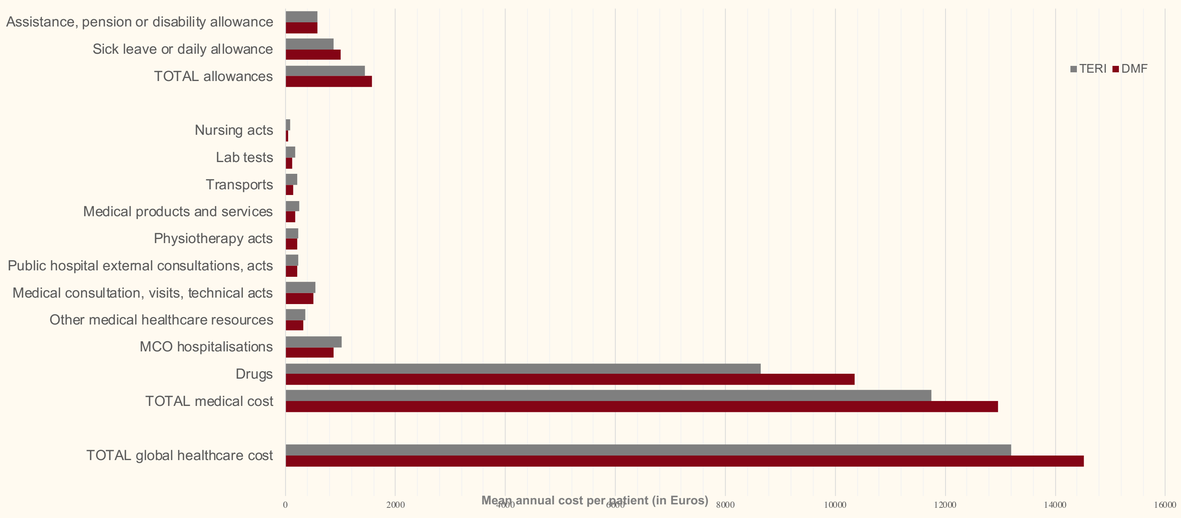

Figure 2. Distribution of the global resource costs during the first index treatment exposure according to the collective perspective in DMF and TERI groups

- **Annual global cost DMF *versus* IMM**

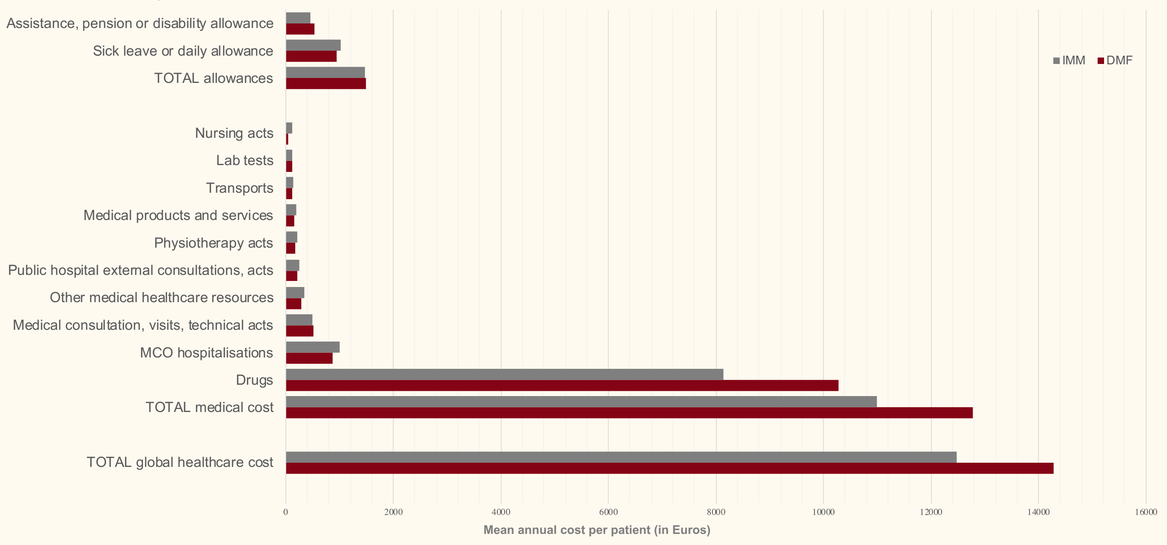

Figure 3. Distribution of the global resource costs during the first index treatment exposure according to the collective perspective in DMF and IMM groups

- **Annual global cost DMF *versus* FTY**

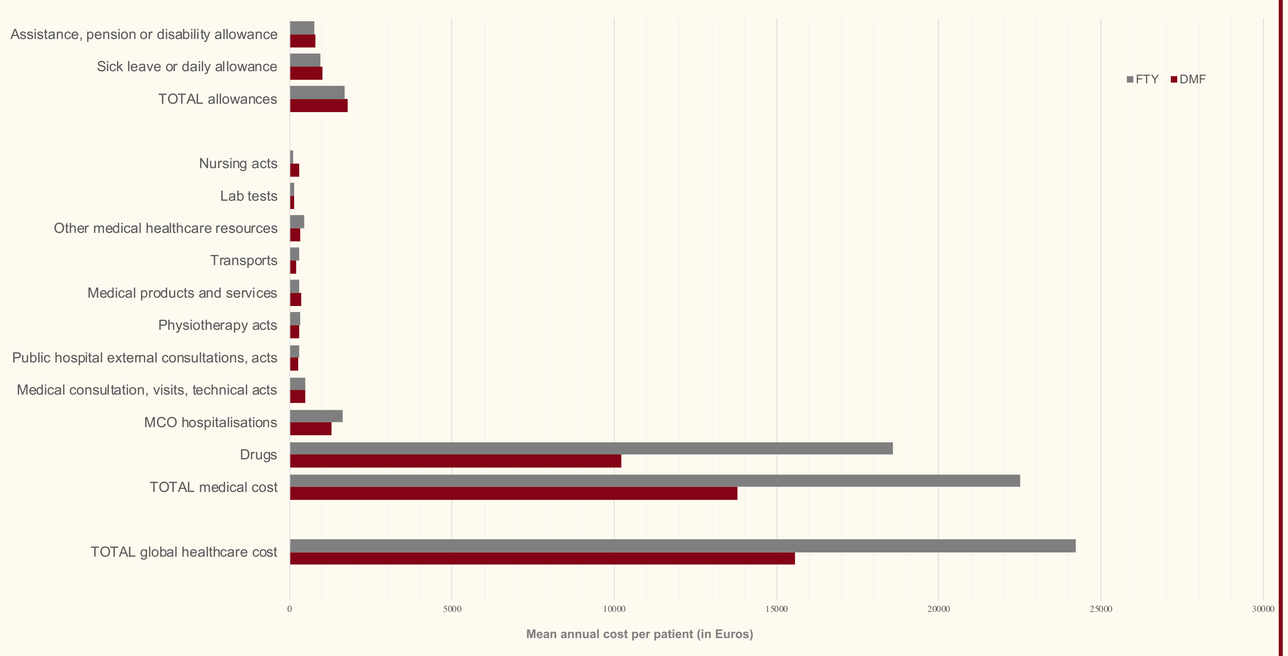

Figure 4. Distribution of the global resource costs during the first index treatment exposure according to the collective perspective in DMF and FTY groups

- **Annual specific cost (costs of all healthcare expenditures) in treatment groups**

Table 1. Specific healthcare resource costs during the first index treatment exposure period according to the collective perspective in each treatment groups

	DMF N = 1679	TERI n = 1679	DMF N = 1780	IMM n = 1780	DMF N = 376	FTY n = 376
Annual total specific medical (in €) Mean (±SD)	11056 (5007)	9572 (4365)	11016 (5127)	8992 (4541)	11478 (6153)	19960 (10118)
Medical area of expenditures						
MS treatment drugs	10023 (4258)	9296 (3288)	9990 (4260)	7832 (3402)	9876 (4514)	18096 (8292)
MS specific hospitalisations	731 (1999)	863 (2160)	745 (2267)	885 (2468)	1178 (3041)	1462 (5139)
Neurologist medical visits	101 (116)	101 (119)	96 (111)	96 (119)	92 (128)	92 (163)
MS specific lab tests	108 (89)	176 (138)	108 (92)	89 (97)	118 (131)	119 (128)
MS specific medical devices	93 (655)	136 (882)	76 (563)	89 (721)	214 (1096)	191 (1013)

Conclusion

- **Compared to TERI and IMM:**
  - **DMF** is an effective treatment strategy **in reducing relapse occurrence** in MS patients
  - DMF entails **an additional cost from the collective perspective** mostly explained by the **price of the drug** itself.
- **FTY** involves **higher specific medical costs** than those of other MS drugs, which may be explained by the more severe clinical profile of MS patients treated with this drug.

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