

THE ECONOMIC BURDEN OF NONTUBERCULOUS MYCOBACTERIAL PULMONARY DISEASE IN CANADA, FRANCE, GERMANY, AND UNITED KINGDOM

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Background

Nontuberculous mycobacterial pulmonary disease (NTMPD) is a rare but emerging global health concern, with important public health implications.^{1,2} The infection is caused by ubiquitous mycobacteria found in the soil and water.³ Over 150 species of NTM have been identified and *Mycobacterium avium* complex (MAC) has been reported to be the most common causative agent in NTMPD worldwide.³

Treatment of NTMPD consists of a long-term course of multi-drug antibiotic regimen; however, patients who are not responsive to first-line therapy have limited therapy options.¹

Currently, data quantifying the economic burden of NTMPD are sparse,^{4,5} and for patients who are refractory to treatment, the economic burden is unknown.

The study objective was to estimate the economic burden of NTMPD in Canada, France, Germany and the UK, focusing on refractory patients without concomitant cystic fibrosis or tuberculosis, who were infected with MAC.

Methods

Study Design:

We conducted a retrospective observational survey of physicians in Canada, France, Germany, and the United Kingdom (UK), to collect data on health care resource utilization among patients with refractory NTMPD caused by MAC over a 24-month period.

Qualified physicians were referred to eligible patients' charts to complete an online survey. The survey captured anonymized information about patient's treatment history for NTMPD-related health care resource utilization. Physicians were asked to extract the requested information from the medical records for up to 5 eligible patients, living or since deceased, who met all of the eligibility criteria in **Box 1**.

Box 1. Eligibility criteria

- Infected with MAC: *M. avium*, *M. intracellulare*, and/or *M. chimaera*.
- "Refractory" (i.e., received an antimycobacterial treatment with a reasonable level of treatment compliance AND demonstrated one or more positive cultures after at least 6 months of therapy).
- Received some or all treatment any time after September 2013.
- No cystic fibrosis or tuberculosis in the past 24 months
- Primarily under the responding physician's care for management of NTMPD and not referred to another physician for management.

Data relating to medication use and data on diagnostic and post-diagnostic testing for NTMPD were captured from the time of diagnosis to the time of survey completion. Other resource utilization, including hospitalizations, physician visits, ancillary care, and other testing, was captured for the 24 month study period prior to survey completion.

Costing:

We summarized all NTMPD-related resource use and applied unit costs to estimate the total economic burden, from a government health care provider perspective using 2015 EUR (France and Germany), CAD (Canada) and GBP (UK).

Country-specific unit costs were obtained from publicly available sources, literature review, and clinical expert consultation.

Weighting:

We applied previously described method to correct for over- or under-representation of the sampled population against the distribution of the universe of NTMPD patients in each country.⁶ The weighting was informed by previous market research studies and literature-based estimates of the true patient distribution.^{7,8} The factors influencing a patient's weight were: 1) specialty of the treating physician, 2) patient volume of the treating physician, and 3) country of residence.

Results

In total, 63 physicians provided data (18 from Canada; 16 from France; 13 from Germany; 16 from the UK), on a total of 182 patient cases. When pooling the sample across countries, weighted patient counts were: 42 from Canada; 42 from France; 55 from Germany; and 43 from the UK.

Pooled demographic and clinical characteristics of participating physicians and patients are in **Table 1** and **Table 2**. Duration of follow up is summarized in **Table 3**.

Table 1. Physician characteristics

Physician characteristics	N	%
N physicians=63		
Primary specialty (n; %)		
General medicine	11	17.5
Infectious disease	14	22.2
Internal medicine	12	19.0
Pulmonology/respiratory medicine	24	38.1
Other	2	3.2
Number of NTMPD patients managed		
Mean (standard deviation)	20	7.9
Median (range)	20	1 - 30

Table 3. Characteristics of follow-up

Follow-up time	N	%
N patients =182		
Duration of follow-up, in weeks (mean; standard deviation)		
Time from symptom onset to diagnosis of NTMPD	22.2	31.8
Time from diagnosis to end of study period or death	106.7	78.6
Observation time during prior 24 month study period	100.9	14.9

Table 2. Patient demographic characteristics

Patient characteristics	N	%
N patients =182		
Sex (n; %)		
Male	136	74.7
Female	46	25.3
Current age (mean, standard deviation)	59.9	13.9
History of smoking (n; %)		
Yes	132	72.5
No	43	23.6
Unknown	7	3.8
Vital status at end of study period (n; %)		
Alive	150	82.4
Deceased	32	17.6
Comorbid conditions (n; %)		
Bronchiectasis	69	37.9
HIV/AIDS infection	28	15.4
Neither of the above	91	50.0
NTMPD species (n; %)*		
<i>M. avium</i>	115	63.2
<i>M. intracellulare</i>	71	39
<i>M. chimaera</i>	10	5.5
Other	5	2.7

*May add to >100% as patients may have more than one species

Results

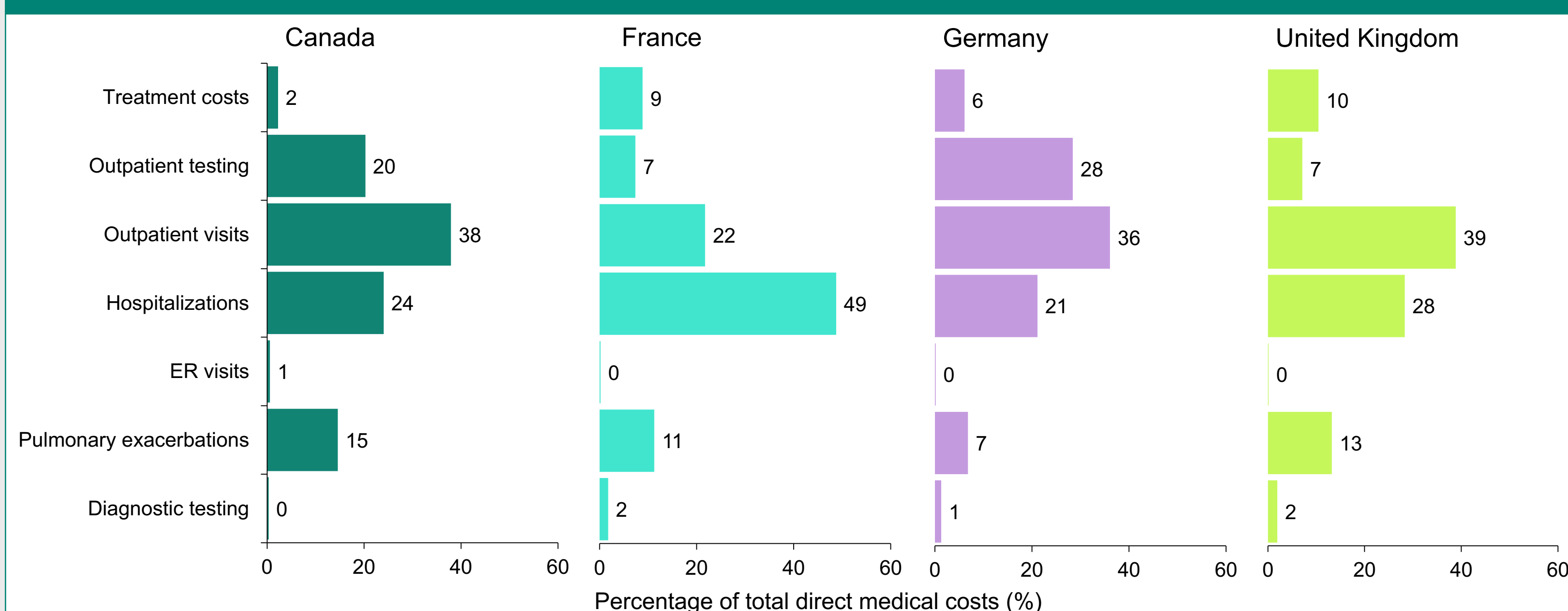


Figure 1. Component costs of NTMPD management: percentage of total direct NTMPD-related medical costs

Note: Types of visits and tests captured within the categories, 'outpatient tests' and 'outpatient visits' are listed in Table 4.

Table 4. Proportion of subjects and average annual utilization of select resources

Unit type	Resource use during 24-month study period								
	Canada n = 42		France n = 42		Germany n = 55		United Kingdom n = 43		
	% with any use*	Mean units**	% with any use*	Mean units**	% with any use*	Mean units**	% with any use*	Mean units**	
Pulmonary Exacerbations									
Required ER visits	Visit	40.6	1.0	11.9	0.8	12.8	1.0	32.2	1.2
Required hospitalizations	Days admitted	28.7	7.9	16.7	16.5	14.6	10.7	29.9	7.0
Required outpatient visit									
Visit in physician's office	Visit	19.1	2.4	14.3	2.2	5.5	1.2	13.8	1.3
IV infusion clinic	Visit	7.2	2.3	0.0	0.0	0.0	0.0	0.0	0.0
Other	Visit	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Any pulmonary exacerbation	-	45.4	-	28.7	-	20.1	-	34.5	-
Other health care utilization (not related to pulmonary exacerbations)									
ER visits	Visit	35.8	1.0	14.3	1.2	14.6	0.8	9.2	1.4
Hospitalizations									
Hospitalization for respiratory infection or inflammation	Days admitted	47.8	8.3	90.8	12.0	74.8	6.8	52.9	8.2
Hospitalization requiring surgery	Days admitted	0.0	0.0	11.9	2.8	0.0	0	2.3	8.9
Outpatient visits									
Physician office visit	Outpatient visit	93.2	5.5	59.7	8.0	43.8	6.4	52.9	4.3
Infusion clinic visit	Outpatient visit	4.8	4.1	2.4	5.1	5.5	3.3	0.0	0.0
Homecare nurse	Outpatient visit	14.8	71.1	40.1	19.1	18.8	60.6	1.3	0.6
Physiotherapy	Outpatient visit	28.1	24.3	55.1	17.6	27.9	10.1	24.4	12.4
Pulmonary rehabilitation	Outpatient visit	32.1	22.6	8.4	8.2	49.4	12.5	60.4	23.4
Other	Outpatient visit	9.8	15.3	6.2	39.2	4.4	9.7	2.0	49.6
Outpatient tests									
Biopsy	Test	4.4	9.3	23.3	2.4	25.3	9.9	11.0	1.9
Sputum specimen	Test	76.6	1.4	71.1	1.8	62.3	1.4	30.3	1.0
Bronchial wash or lavage	Test	21.9	1.8	65.3	1.2	53.8	1.3	77.4	1.6
Blood test	Test	53.1	5.8	82.5	6.0	60.0	6.3	77.5	6.1
Bone scan	Test	2.2	0.6	7.6	3.9	6.2	0.9	1.1	0.4
CT scan	Test	71.0	2.6	83.9	4.9	52.4	10.6	72.3	2.8
ECG	Test	28.6	2.3	44.7	7.4	37.3	5.0	35.8	2.0
MRI	Test	7.6	5.6	21.3	4.1	9.1	28.4	7.9	1.3
Angiography	Test	0.0	0.0	0.0	0	3.7	1.2	0.0	0.0
CT guided biopsy	Test	0.0	0.0	0.0	0.0	3.7	3.5	11.0	1.3
Pulmonary function test	Test	26.0	1.4	12.0	1.0	40.1	4.9	30.4	1.6
Ultrasound	Test	1.3	0.8	32.4	3.0	43.6	10.3	2.7	2.0
X-Ray	Test	75.9	3.6	68.9	5.9	73.2	4.1	76.0	4.1
Other	Test	9.8	1.4	0.0	0.0	6.5	7.4	0.0	0.0

*During the 24-month resource utilization collection period; **Mean annual utilization among subjects with any utilization of that resource within the prior 24 months. Abbreviations: CT = computed tomography; ECG = electrocardiogram; ER = emergency room; IV = intravenous; MRI = magnetic resonance imaging

Table 5. Annual NTMPD-related direct medical costs per patient in Canada, France, Germany and the UK

Country	Annual direct medical cost per patient			
	Mean	Standard deviation	Median	Range
Canada (2015 CAD)	27,058	(31,960)	19,202	(811 - 236,770)
France (2015 EUR)	13,442	(16,912)	8,457	(2,055 - 80,992)
Germany (2015 EUR)	9,500	(10,875)	5,919	(4 - 48,910)
United Kingdom (2015 GBP)	13,009	(11,623)	8,616	(99 - 43,592)

Discussion

This study captured detailed data on NTMPD-related resource utilization based on patient charts for a relatively large cohort of patients with refractory NTMPD caused by MAC. The data for this study came directly from the charts of physicians who regularly manage NTMPD. The physicians were sampled from various settings, specialties, and geographic regions, allowing the study to provide nationally representative results.

A core challenge of chart reviews is missing or incorrectly extracted or entered data, which was indeed a limitation of the current study. Physicians were asked to state NTMPD-specific healthcare resource use, and we could not verify how accurately this was done. In addition, patient selection may have influenced the results. Costs were namely highly right-tailed, in which some patients had very high costs, and they may have been under- or over-represented in our sample.

Conclusions

Based on the findings of this study, we conclude that managing patients with refractory NTMPD caused by MAC is associated with substantial resource use, with annual cost per patient exceeding costs reported elsewhere for other respiratory conditions, such as asthma, chronic obstructive pulmonary disease or tuberculosis.^{9, 10, 11}

Disclosures

Sarah Goring, Nancy Risebrough, Ben Wilson and Janice Watch are employees of ICON plc. Jack R. Gallagher, Kylee J. Heap and Susan Carroll are employees of Clarity Pharma Research LLC. Marko Obradovic is an employee of Insmmed Germany GmbH. Insmmed Incorporated (Bridgewater, NJ) funded this research.

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