Towards Diagnosing Rare Diseases: Referral Behavior of Physicians in Europe

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Introduction

- Rare disease patients and their families face significant challenges, with the most crucial one being the difficulty in getting a definitive diagnosis.[1]
- This is often due to misdiagnoses, delayed diagnoses, and a lengthy diagnostic journey[2], partly caused by low rare disease awareness among physicians.[3]
- Understanding how primary care physicians and specialists refer patients with undiagnosed symptoms could play an important role in achieving early and accurate diagnoses, which could substantially impact the course of the disease.

Objective

To investigate the referral behavior of primary care physicians (PCPs) and specialists when encountering patients with undiagnosed symptoms.

Methods

Physicians (including PCPs and specialists) were recruited via physician panels to participate in a cross-sectional survey.

The web-based survey was conducted during January 2023 in France, Germany, Italy, Spain, and United Kingdom (UK).

Results

In total, 1,610 physicians in Europe participated (478 PCPs and 1,132 specialists). *Table 1* displays the numbers and percentages of physicians by country and medical specialty.

When faced with symptoms for which they cannot find a diagnosis, 11.9% of PCPs and 24.7% of specialists frequently suspected a rare disease. Neurologists (41.4%) are more inclined to suspect a rare disease than other specialists *(Figure 1)*.

As shown in *Figure 2*, when unable to diagnose a disease, physicians referred patients after the:

- **Initial visit** (16.0% overall, 11.1% PCPs, 18.1% specialists)
- **Second visit** (43.7% overall, 42.5% PCPs, 44.2% specialists)
- **Third or later visit** (40.3% overall, 46.5% PCPs, 37.7% specialists)

Physicians reported different reasons for referral delay (after the second visit or later) (*Figure 3*)

Primary reasons for waiting to refer patients until after at least their second visit varied by:

- **Medical specialty**
  - Waiting for (or inconclusive) test results differed by specialty as shown in *Figure 4*
- **Country (Figure 5)**
  - Waiting for (or inconclusive) test results (range: 42.1% Germany, 58.3% Italy)
  - Preferring to wait/watch (range: 9% Italy, 21% France)
  - Delays in scheduling appointments with other physicians (range: 9.9% Italy, 18.5% Germany)

Secondary reasons for referral delays varied by:

- **Types of Physicians (Figure 6)**
  - Symptoms not being applicable to the physician/not wanting to interfere (PCPs: 4.2; specialists: 10.9; p<0.001)
  - Long waiting lists (54.6 PCPs, 37.3 specialists, p<0.001)
- **Country (Figure 7)**
  - Desire of patients to not see another physician (range: 10.0 UK, 33.8 Germany)
  - Symptoms not applicable to physician/not wanting to interfere (range: 4.3 Italy, 16.2 Germany)
  - Scheduling complexities/paperwork (range: 7.3 France, 17.6 Spain)

Abbreviations

PCP = Primary care physician

Table 1: *Participating physicians: Numbers and percentages overall, by country and medical specialty*

Medical Focus	Overall (N=1,610)		France (N = 193)		Germany (N = 243)		Italy (N = 422)		Spain (N = 518)		UK (N = 234)	
	n	%	n	%	n	%	n	%	n	%	n	%
Primary care	478	29.7	61	31.6	62	25.5	92	21.8	138	26.6	125	53.4
Specialties												
Hematology/ Oncology/HemOnc	176	10.9	16	8.3	10	4.1	68	16.1	70	13.5	12	5.1
Internal Medicine	112	7.0	10	5.2	34	14.0	23	5.5	41	7.9	4	1.7
Cardiology	106	6.6	18	9.3	19	7.8	40	9.5	17	3.3	12	5.1
Neurology	99	6.1	13	6.7	16	6.6	28	6.6	35	6.8	7	3.0
Pediatrics	88	5.5	16	8.3	14	5.8	13	3.1	39	7.5	6	2.6
Dermatology	82	5.1	4	2.1	27	11.1	23	5.5	25	4.8	3	1.3
Eye Care – Ophthalmology	77	4.8	10	5.2	9	3.7	17	4.0	29	5.6	12	5.1
Endocrinology & Diabetology	77	4.8	9	4.7	5	2.1	30	7.1	21	4.1	12	5.1
Rheumatology	71	4.4	9	4.7	3	1.2	25	5.9	22	4.3	12	5.1
Gastroenterology/Hepatology	67	4.2	8	4.2	3	1.2	26	6.2	27	5.2	3	1.3
Obstetrics & Gynecology	63	3.9	5	2.6	16	6.6	3	0.7	23	4.4	16	6.8
Urology	53	3.3	3	1.6	14	5.8	17	4.0	14	2.7	5	2.1
Nephrology	41	2.5	10	5.2	9	3.7	4	1.0	15	2.9	3	1.3
Infectious Diseases (includes HIV)	20	1.2	1	0.5	2	0.8	13	3.1	2	0.4	2	0.9

Figure 1: *Percentage of physicians who often suspect a rare disease when unable to diagnose symptoms by medical specialty.*

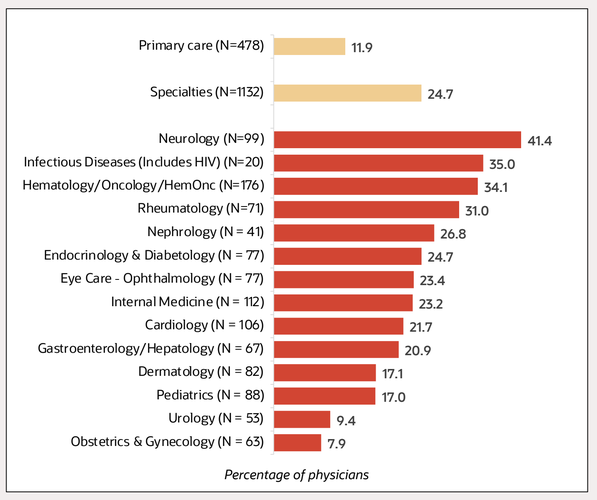


Figure 2: *Number of consultations before the undiagnosed patient is referred to another physician (percentage of physicians)*

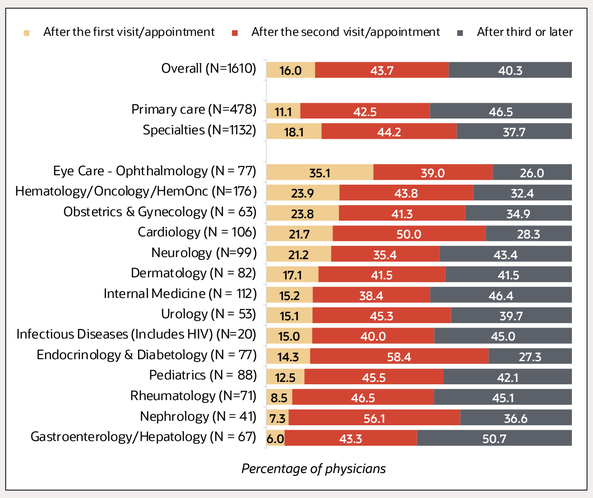


Figure 3: *Primary and secondary reasons for referral delay* ***(after the second visit or later): Percentage of physicians overall***

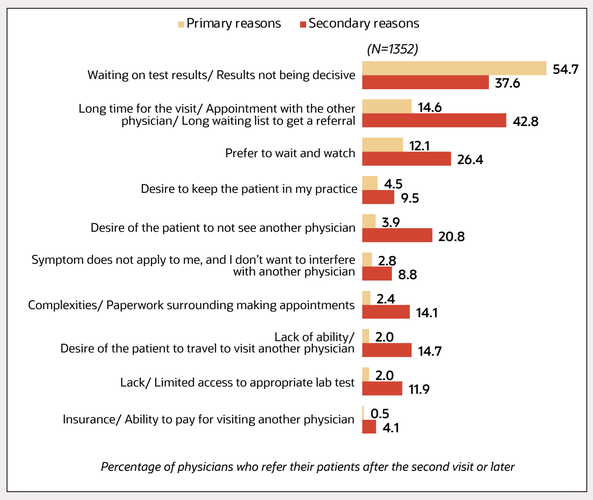


Figure 4: *Waiting for (or inconclusive) test results:* ***Percentage of physicians by medical specialty.***

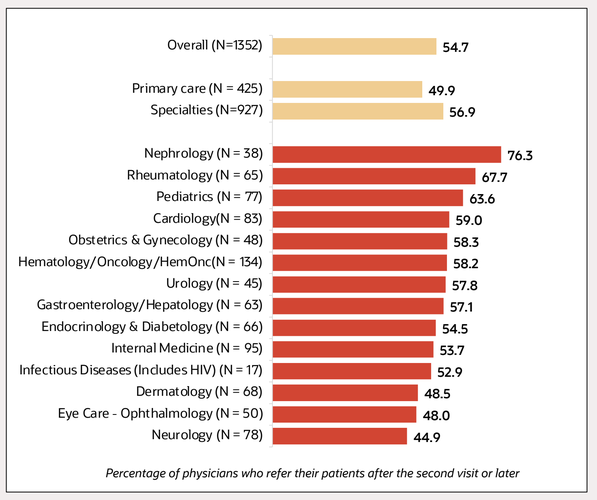


Figure 5: *Primary reasons for referral delay* ***(after the second visit or later)*** *by country: Percentage of physicians by country*

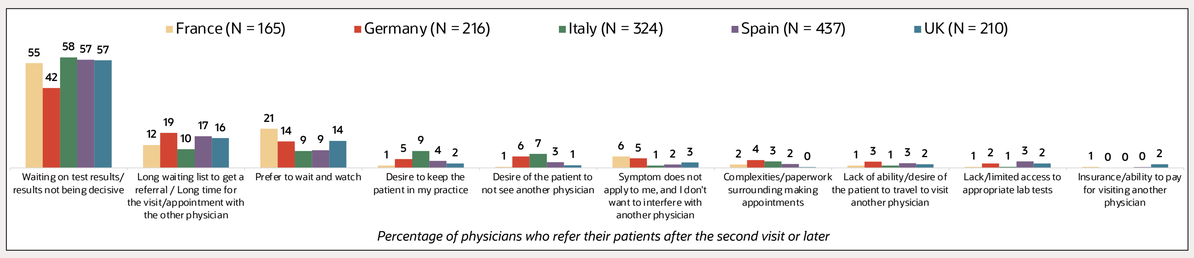


Figure 7: *Secondary reasons for referral delay* ***(after the second visit or later)****: Percentage of physicians by country.*

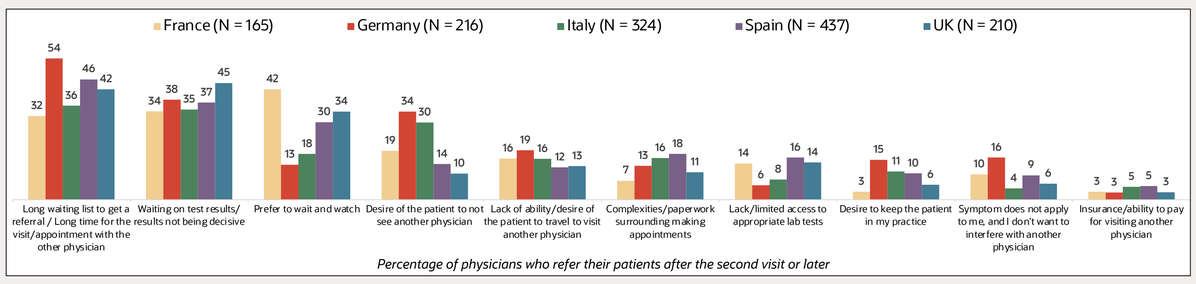
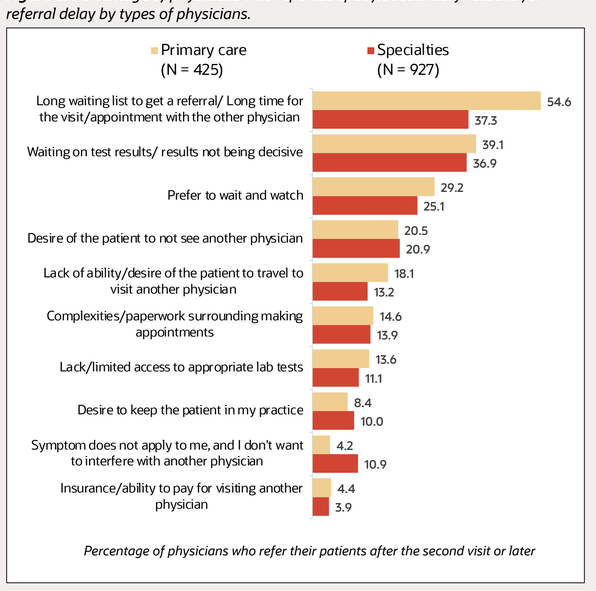


Figure 6: *Percentage of physicians who reported specific secondary reasons for referral delay by types of physicians.*



Conclusion

- Differences in referral behavior exist among PCPs and specialists, within specialties, and across countries.
- PCPs are far less likely than specialists to suspect a rare disease when encountering symptoms they cannot diagnose.
- Specialists tend to refer patients after the initial visit more often than primary care physicians, when unable to diagnose a disease.
- Waiting for (or inconclusive) test results is the main reason for referral delay, followed by long waiting lists and preferring to watch and wait.
- Improved referral procedures could potentially benefit patient care by reducing time to diagnosis.

References

1. Yan, X.; He, S.; Dong, D. Determining How Far an Adult Rare Disease Patient Needs to Travel for a Definitive Diagnosis: A Cross-Sectional Examination of the 2018 National Rare Disease Survey in China. Int. J. Environ. Res. Public Health 2020, 17, 1757. https://doi.org/10.3390/ijerph17051757
2. Eurordis. "Survey of the Delay in Diagnosis for 8 Rare Diseases in Europe ('EURORDISCARE 2')." Fact sheet EurordisCare 2 (2007).
3. Vandeborne, L., van Overbeeke, E., Dooms, M. et al. Information needs of physicians regarding the diagnosis of rare diseases: a questionnaire-based study in Belgium. Orphanet J Rare Dis 14, 99 (2019). https://doi.org/10.1186/s13023-019-1075-8

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