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ORIGINAL ARTICLE

Patients' perception on the quality of care for multiple endocrine neoplasia disorders in Europe: an online survey from a patient support group

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Abstract

Purpose European Patient Advocacy Groups (ePAGs) within the Endo-ERN identified a lack of knowledge about quality of care (QoC) of patients with multiple endocrine neoplasia (MEN). The aim of this study was to identify inequalities in care and to encourage improvements.

Methods The European MEN Alliance (EMENA) developed and conducted a survey, using the European Commissions' EUSurvey platform. Patient groups and healthcare professionals (HCPs) distributed the survey.

Results A total of 288 participants completed the survey (MEN1 $n = 203$, MEN2 $n = 67$, MEN3 $n = 18$) from 18 European countries. The majority of respondents were recruited via patient groups (58%), aged between 41 and 60 years (53%) and were female (67%). All participants reported having been diagnosed on average 5.58 years (95%-CI: 4.45–6.60) after first symptoms occurred. This timeframe was lower in the group with MEN2 (2.97 years, 95%-CI: 1.37–4.57). Most of the participants (67%) received their diagnosis by a positive gene test after presenting with one or more MEN-related tumours. Overall QoC was rated as either "good" (43%) or "excellent" (36%).

Conclusion The results of this unique Europe-wide, patient-driven survey on QoC of patients with MEN show that ratings for overall QoC were lower than ratings for different aspects of care. This may be because of the complex nature of care for genetic syndromes. Furthermore, patients who connect with patient groups may be deemed "expert patients" whose answers are not representative of the overall MEN patient community. We hope that Endo-ERN can support further education and training for HCPs based on these results.

Keywords Multiple endocrine neoplasia · Quality of care · Patient report · Endocrine tumours · Rare diseases

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Introduction

Multiple endocrine neoplasia (MEN) syndromes cause a genetic predisposition in a person to develop tumours involving at least two endocrine glands. Until now, four types of MEN disorders have been identified, called MEN1, MEN2 (formerly MEN2a), MEN3 (formerly MEN2b) and MEN4 (also known as MENX). Each syndrome is characterised by the occurrence of different tumours over time. Parathyroid, pituitary and pancreatic islet cell tumours regularly occur in MEN1. Parathyroid hyperplasia, medullary thyroid carcinoma (MTC) and pheochromocytoma are specific for MEN2. MTC, pheochromocytoma and a Marfanoid appearance in MEN3. MEN4 is characterized with parathyroid and anterior pituitary tumours in connection with tumours of the kidneys, adrenals and the reproductive system. All MEN syndromes are inherited as autosomal dominant disorders [1–12]. MEN1 is the result of a gene mutation on chromosome 11q13 of the "*Menin*" gene, while MEN2 is characterized by a failure of the "rearranged during transfection" (*RET*) gene [13–15]. Most of the studies published so far focus on genetics [2, 3, 16–19], screening and diagnostics [20, 21] or therapeutic aspects [4, 5, 22, 23]. A few studies report on quality of life [22, 24–30] but there have been no studies so far on quality of care (QoC) in MEN patients. However, patients and patient groups are interested in QoC and equality of care throughout Europe. Patient-oriented research is important and currently on the rise [31–33]. So far, there is no concrete, verifiable evidence of their benefit [34]. Nevertheless, patient-driven research, particularly in rare diseases, can contribute to faster research because of the "unique motivations and research approach[es]" [35] of patient groups.

The establishment of the European Reference Networks (ERNs) for Rare Diseases, including the European Reference Network on Rare Endocrine Conditions (Endo-ERN) in 2017, was intended to improve the care of rare disease patients living in the European Union. This requires an assessment of the current status, the needs and the differences in the care of patients with MEN syndromes that goes beyond anecdotal description. For example, which components of care are successful in one country and could improve care in another country? In the MTG 4 (main thematic group "Genetic Endocrine Tumour Syndromes") of the Endo-ERN, country-specific differences in care have been identified, for example, in the development of guidelines.

The objective of our project was to perform a first investigation of patient-reported perceived QoC in MEN syndromes in Europe through a patients for patients research approach.

Materials and methods

In a participatory process, members (mostly patient advocates) of the multinational umbrella group, European Multiple Endocrine Neoplasia Alliance (EMENA), developed an online questionnaire to gather patient-reported aspects on perceived QoC. This unique questionnaire contained 29 questions in sections about sociodemographics, participants' disease experience, access and use of healthcare services, trust, adherence, decision-making and satisfaction with care in general. The questionnaire was designed by patients for patients. Afterwards, we performed paper-based and online pre-tests regarding the feasibility of the survey. Volunteer native speakers of several patient groups translated our final English draft into French, Spanish, Italian, Dutch and German languages. We chose this approach to harness the familiarity of these individuals with the specific medical terminology in their language. We implemented the final version of the survey on the European Commissions' EUSurvey platform [36]. Distribution of the survey was done through EMENA national member groups in the UK, Belgium, The Netherlands, Italy and Germany and affiliated groups in France, as well as through Endo-ERN European Patient Advocacy Groups and other rare diseases associations in all EU-28 countries, mostly via mailing lists, social media or other online channels. We conducted the survey between March and May 2018. Informed consent was obtained by every participant in advance by actively agreeing on the terms of the survey. In case of patients younger than 18 years, we encouraged the legal guardians to complete the survey on their behalf. The survey was conducted anonymously. We did not collect any data that would allow us to identify any individual participant. If there were fewer than five participants from one country, we did not consider these cases individually for further analysis but have grouped them under "other countries".

Variables used for analyses

The variables considered for our analyses can be found in Table 1.

Data management and analyses

We extracted and downloaded data from the EUSurvey platform and performed data cleaning afterwards. We checked our data for plausibility by using the "unusual cases" function in SPSS and completed further checks on consistency of the data. Information on the timespan from symptoms to diagnosis was limited to 40 years, resulting in three implausible values (50/100/100 years) which were set to missing as no clarification was possible due to anonymization. No further exclusions or corrections had to be made. Statistical analyses were undertaken using SAS 9.0

Table 1 Variables of the survey considered for analyses

Variable	Characteristics
Country of residence	Name of country (all EU-28 countries were available to select)
Gender	Male, female, prefer not to answer, no answer
Type of MEN	1, 2a, 2b, 4, no answer
Age in eight groups	0–9, 10–18, 19–30, 31–40, 41–50, 51–60, 61–70, 70+, no answer
Year of diagnosis	1900–2017
Diagnosis of MEN	Based on a gene test because a family member was diagnosed with MEN, but I have not had any symptoms or MEN-related endocrine tumours yet / I have had MEN-related endocrine tumours and a positive gene test with genetic mutation / I have had MEN-related endocrine tumours and a negative gene test without genetic mutation / I have had MEN-related endocrine tumours but have not had a gene test/no answer
Timespan from first MEN-related symptoms until diagnosis	Years
Healthcare professional (HCP) in charge of MEN care	Family doctor (GP), endocrinologist, oncologist, surgeon, gastroenterologist, neuroendocrinologist, geneticist, psychiatrist/psychologist, cardiologist, neurologist, pharmacologist, respiratory physician, other, "I don't know"
Level of healthcare provider	Primary physician/family doctor, district/regional hospital, specialist reference centre
Access to a specialist endocrine nurse	Yes, no, don't know
Rating of overall care	Very poor, poor, average, good, excellent (5-point Likert scale)
Amount of time with HCP to discuss MEN-related care	More than enough, right amount, not the time I need
The feeling of ∘Being listened to by HCPs ∘Being involved in decisions made by HCPs ∘Having a knowledgeable medical team ∘Being able to trust the medical team	I strongly agree, I agree, neither agree nor disagree, I disagree, I strongly disagree (5-point Likert scale)

(SAS Institute, Cary NC, USA) and SPSS 25 (IBM, Armonk NY, USA). We computed point and interval estimates with respective confidence intervals, where appropriate. We did not perform any formal hypothesis testing due to the nature of our survey.

Results

Characteristics of the study population

A total of 288 participants completed the survey (MEN1 $n = 203$, MEN2a $n = 67$, MEN2b/3 $n = 18$) from 18 European countries (36% UK, 19% Italy, 16% The Netherlands, 12% Germany, 7% France, 10% other). The majority of respondents were female (67%) and knew about the survey via patient groups (58%). Participants were aged between 0 and 70+ years old and the majority (53%) were aged 41–60 years. There were no differences by gender regarding age. More characteristics by type of MEN disorder are shown in Table 2.

Diagnoses of MEN

All participants reported to have been diagnosed on average 5.4 years (95%-CI: 4.5–6.6) after first symptoms occurred. This mean timespan was shorter in the group with MEN2 (2.9 years, 95%-CI: 1.4–4.6), more details are shown in Table 3. There was also a shorter mean timespan among participants with a previous positive family history and a therefore performed gene test: 3.1 years (95%-CI: 1.6–4.6) vs. 6.1 years (4.9–7.3). Most of the participants (67%) were diagnosed by a positive gene test after presenting with one or more MEN-related tumour. More women than men (68%) were among all participants affected by MEN disorders (56% in MEN3 patients).

Perception of QoC

Participants were mainly treated by an endocrinologist (77%) in a specialist reference centre (65%). Only 42% reported having access to a specialist endocrine nurse. This percentage differed widely between European countries, see Table 4. Most participants reported having just the right amount of time to talk to their doctor about their MEN care (73%), felt listened to (85%) and felt involved in decisions about their care (81%). The majority believed that their medical team was well informed about MEN (84%) and trusted their medical team (85%). Regional differences are shown in Table 4. Overall QoC was rated as either "good" (43%) or "excellent" (36%). Results for MEN1 differed slightly from those for MEN2 or MEN3 ("excellent" 25%

Table 2 Characteristics of the study population by type of MEN syndrome

	MEN1	MEN2	MEN3	Total
n	203 (69% female)	67 (67% female)	18 (56% female)	288 (68% female)
Most frequent age group	41–50 years	51–60 years	19–40 years	41–50 years
Mean timespan from first symptoms to diagnosis, mean ± std. (range)	6.2 ± 9.0 (0–38)	3.0 ± 6.5 (0–34)	5.1 ± 8.3 (0–17)	5.4 ± 8.4 (0–38)

Table 3 Timespan (mean and standard deviation) from first symptoms to diagnosis by country, and *n* for all answers shown per country, respectively (only countries with five or more participants)

Country	Timespan (years)	*n*
Belgium	5.7 ± 12.7	7
France	6.7 ± 10.2	19
Germany	7.0 ± 9.2	33
Italy	6.1 ± 9.3	56
The Netherlands	4.7 ± 8.0	46
Spain	3.8 ± 3.0	5
UK	4.8 ± 7.6	103
All	5.4 ± 8.4	285

vs. 40 and 44%, respectively; "good" 46% vs. 30 and 50%, respectively). Further reported quality indicators are shown in Table 4.

Discussion

To our knowledge, this is the first study about QoC aspects in MEN syndromes in Europe. We present findings of an online survey among 288 participants from 18 different European countries who were recruited via patient groups all over Europe using different methods. We developed and translated our survey among our multinational umbrella patient group. Even though our questionnaire has not been validated, we believe that our approach to analyse the QoC of MEN patients is a valuable first step in bringing about improvements in care for MEN patients.

In line with previous findings [37, 38], more women than men engage with patient advocacy groups and actively take part in surveys, so more females than males are represented in our survey.

The lower timespan from first symptoms to diagnosis in MEN2 patients (3 years) vs. MEN1 patients (6 years) might be a result of completely different courses of the diseases and diagnostic approaches, respectively: in MEN2, a thyroid screening usually reveals nodules that are quickly identified as cold nodules using a scintigram. Because this is a tumour disease, these patients are assessed much more thoroughly and this might lead to an earlier diagnosis of MEN2 [5, 26]. On the other hand, the clinical picture of MEN1 is much more varied, and at the beginning of the disease, before the exact diagnosis is made, it points to many more different clinical pictures [2]. The lower timespan from first symptoms to diagnosis in patients with a positive family history (3 vs. 6 years) can certainly be explained in part by genetic testing. We were not able to determine why it still takes an average of 3 years until a diagnosis is made in this group.

The trend for lower ratings regarding the overall QoC by participants with MEN1 might be connected to a perceived longer "diagnostic odyssey" in MEN1. Patients need to consult many different healthcare specialists (internists, endocrinologists, oncologists, gastroenterologists) up to their diagnosis. These ratings could further be related to the fact that patients do not feel they are taken seriously enough during this "odyssey".

Access to a specialist endocrine nurse varies widely between different countries, most probably due to different health systems. Specialist endocrine nurses are an important link between doctors and patients to support patients along their complex path through medical care not only medically but also emotionally and psychologically [39]. As there is no evidence on availability of endocrine nurses in Europe or a comparison between EU member states, it is speculative to discuss those differences. However, specialist nurses are, in general, considered to contribute to a higher patient satisfaction [40].

Unfortunately, contrary to our expectations, the response rate from Spain and Portugal was low, although local patient representatives were highly committed to promote our survey. No citizens of eastern European countries participated in our survey, as the patient organizations are rare or non-existent and language barriers are still a major challenge. Therefore, we already see this under-representation as a further indication of the inequality in the care of MEN patients across Europe. We hope that with the increasing establishment and expansion of Endo-ERN, cooperation with the patients there can be established.

Uniqueness of our project

This research project was planned and conducted in a participatory process driven by patients, supported by doctors

Table 4 Reported quality indicators for different countries, *n* for all answers shown per country respectively in alphabetical order (only countries with five or more participants) and 95% CIs in brackets

Country	Access to an endocrine nurse (rel. %)	Participants' perception about the knowledge of their respective healthcare providers on MEN (% of strongly agree and agree)	Participants' trust in their medical team (% of strongly agree and agree)	Overall perceived quality of care by country (relative % of good and excellent rating)	*n*
Belgium	0 (0.0–41.0)	100 (59–100)	86 (42.1–99.6)	57 (18.4–90.1)	7
France	16 (3.4–39.6)	68 (43.4–87.4)	68 (43.4–87.4)	79 (54.4–93.9)	19
Germany	9 (1.9–24.3)	67 (48.2–82)	64 (45.1–79.6)	30 (15.6–48.7)	33
Italy	38 (24.9–51.5)	98 (90.4–100)	93 (82.7–98)	75 (61.6–85.6)	56
The Netherlands	52 (26.9–67.1)	96 (85.2–99.5)	96 (85.2–99.5)	89 (76.4–96.4)	46
Norway	20 (0.5–71.6)	40 (5.3–85.3)	40 (5.3–85.3)	20 (0.5–71.6)	5
Spain	60 (14.7–94.7)	100 (47.8–100)	100 (47.8–100)	80 (28.4–99.5)	5
UK	58 (48.1–67.9)	83 (73.8–89.3)	83 (73.8–89.3)	80 (70.5–86.9)	103
Other[a]	43 (17.7–71.1)	71 (41.9–91.6)	64 (35.1–87.2)	64 (35.1–87.2)	14
All	42 (36.2–47.9)	84 (79.7–88.4)	82 (79.7–88.4)	72 (66.7–77.3)	288

[a]Croatia, Denmark, Estonia, Finland, Greece, Ireland, Poland, Portugal, Sweden and Switzerland

and scientists from several European countries. Our collaborative project of patient groups across Europe on a rare disease topic seems to be exclusive so far as research was conducted from patients about patients for patients.

Conclusion

This project shows that MEN patients in Europe generally consider the quality of their care to be of a high standard. Depending on the type of endocrine disorder, differences in the perception of QoC could be taken into account when updating medical guidelines. However, qualitative research might be necessary to investigate further aspects regarding the patients', their relatives' and healthcare professionals' perspectives on this matter. Our pan-European project might encourage clinicians and scientists across Europe to further intensify their cooperation in research on MEN. The setting up of the European Registries for Rare Endocrine Conditions project within the Endo-ERN is an important first step. As these tumour syndromes are rare, there are always only a few patients per country or study centre. It is important to take advantage of the opportunities offered by cross-border cooperation. In particular, the establishment and integration of the Endo-ERN network structure into the respective national healthcare systems might lead to improvements in the care of MEN patients and also to a harmonization of the QoC on a common wider European level.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Author contributions K.P.D. performed data analysis, interpreted the results and wrote the manuscript. P.B., J.G. and L.S. contributed to the interpretation of the results and to writing the manuscript. K.P.D., P. B., J.G., J.P., M.S., M.A., D.v.G. and L.S. had the idea for the project and designed the questionnaire. J.P. and M.-L.B. contributed to interpreting the results and writing the manuscript. All authors reviewed the manuscript and approved it for submission.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest. J.G. and P.B. are European Patient Advocacy Group patient representatives and co-chairs of the main thematic group (MTG) 4 (Genetic Endocrine Tumour Syndromes) of the European Reference Network on Rare Endocrine Conditions (Endo-ERN).

Ethics statement The multinational umbrella group, European Multiple Endocrine Neoplasia Alliance (EMENA), planned and executed this study as a collaborative way for the various patient groups (EMENA members) to assess patients' perspectives on quality of care rather than as an academic or medical research study. The authors therefore did not seek ethics approvals. The authors did not collect personal data of participants that would allow them to identify participants despite their topic being about rare diseases. All participants were asked for their consent to publish the results of the survey. The data collection covers 18 out of the 28 EU member states primarily due to the lack of participatory patient representation in some countries. The authors collected anonymized data thus complying with EU General Data Protection Regulations.

References

1. R.V. Thakker, Multiple endocrine neoplasia-syndromes of the twentieth century. J. Clin. Endocrinol. Metab. **83**(8), 2617–2620 (1998)
2. R.V. Thakker, Multiple endocrine neoplasia type 1 (MEN1) and type 4 (MEN4). Mol. Cell Endocrinol. **386**(1–2), 2–15 (2014). https://doi.org/10.1016/j.mce.2013.08.002
3. M.C. Pacheco, Multiple endocrine neoplasia: a genetically diverse group of familial tumor syndromes. J. Pediatr. Genet. **5**(2), 89–97 (2016). https://doi.org/10.1055/s-0036-1579758
4. G.V. Walls, Multiple endocrine neoplasia (MEN) syndromes. Semin. Pediatr. Surg. **23**(2), 96–101 (2014). https://doi.org/10.1053/j.sempedsurg.2014.03.008
5. J.E. McDonnell, M.L. Gild, R.J. Clifton-Bligh, B.G. Robinson, Multiple endocrine neoplasia: an update. Intern. Med. J. **49**(8), 954–961 (2019). https://doi.org/10.1111/imj.14394
6. F. Marini, A. Falchetti, F. Del Monte, S. Carbonell Sala, A. Gozzini, E. Luzi, M.L. Brandi, Multiple endocrine neoplasia type 1. Orphanet J. Rare Dis. **1**, 38 (2006)
7. F. Marini, A. Falchetti, F. Del Monte, S. Carbonell Sala, I. Tognarini, E. Luzi, M.L. Brandi, Multiple endocrine neoplasia type 2. Orphanet J. Rare Dis. **1**, 45 (2006)
8. A. Falchetti, F. Marini, E. Luzi, F. Giusti, L. Cavalli, T. Cavalli, M.L. Brandi, Multiple endocrine neoplasia type 1 (MEN1): not only inherited endocrine tumors. Genet. Med. **11**(12), 825–835 (2009)
9. J. Moline, C. Eng, Multiple endocrine neoplasia type 2: an overview. Genet. Med. **13**(9), 755–764 (2011). https://doi.org/10.1097/GIM.0b013e318216cc6d
10. J.T. Pang, R.V. Thakker, Multiple endocrine neoplasia type 1 (MEN1). Eur. J. Cancer **30A**(13), 1961–1968 (1994)
11. A. Calender, P. Goudet, Multiple endocrine neoplasia type 1. MEN1—Wermer syndrome. Ann. Endocrinol. **64**(5 Pt 1), 383–388 (2003).
12. A.F. Scarsbrook, R.V. Thakker, J.A. Wass, F.V. Gleeson, R.R. Phillips, Multiple endocrine neoplasia: spectrum of radiologic appearances and discussion of a multitechnique imaging approach. Radiographics **26**(2), 433–451 (2006)
13. F. Khatami, S.M. Tavangar, Multiple endocrine neoplasia syndromes from genetic and epigenetic perspectives. Biomark. Insights **13**, 1177271918785129 (2018). https://doi.org/10.1177/1177271918785129
14. S.C. Chandrasekharappa, S.C. Guru, P. Manickam, S.E. Olufemi, F.S. Collins, M.R. Emmert-Buck, L.V. Debelenko, Z. Zhuang, I. A. Lubensky, L.A. Liotta, J.S. Crabtree, Y. Wang, B.A. Roe, J. Weisemann, M.S. Boguski, S.K. Agarwal, M.B. Kester, Y.S. Kim, C. Heppner, Q. Dong, A.M. Spiegel, A.L. Burns, S.J. Marx, Positional cloning of the gene for multiple endocrine neoplasia-type 1. Science **276**(5311), 404–407 (1997). https://doi.org/10.1126/science.276.5311.404
15. L.M. Mulligan, B.A. Ponder, Genetic basis of endocrine disease: multiple endocrine neoplasia type 2. J. Clin. Endocrinol. Metab. **80**(7), 1989–1995 (1995). https://doi.org/10.1210/jcem.80.7.7608246
16. L. Schaaf, J. Pickel, K. Zinner, U. Hering, M. Hofler, P.E. Goretzki, F. Spelsberg, F. Raue, A. von zur Muhlen, H. Gerl, J. Hensen, D.K. Bartsch, M. Rothmund, U. Schneyer, H. Dralle, M. Engelbach, W. Karges, G.K. Stalla, W. Hoppner, Developing effective screening strategies in multiple endocrine neoplasia type 1 (MEN 1) on the basis of clinical and sequencing data of German patients with MEN 1. Exp. Clin. Endocrinol. Diabetes **115**(8), 509–517 (2007)
17. M.C. Lemos, R.V. Thakker, Multiple endocrine neoplasia type 1 (MEN1): analysis of 1336 mutations reported in the first decade following identification of the gene. Hum. Mutat. **29**(1), 22–32 (2008)
18. A. Machens, L. Schaaf, W. Karges, K. Frank-Raue, D.K. Bartsch, M. Rothmund, U. Schneyer, P. Goretzki, F. Raue, H. Dralle, Age-related penetrance of endocrine tumours in multiple endocrine neoplasia type 1 (MEN1): a multicentre study of 258 gene carriers. Clin. Endocrinol. **67**(4), 613–622 (2007)
19. J.M. de Laat, R.B. van der Luijt, C.R. Pieterman, M.P. Oostveen, A.R. Hermus, O.M. Dekkers, W.W. de Herder, A.N. van der Horst-Schrivers, M.L. Drent, P.H. Bisschop, B. Havekes, M.R. Vriens, G.D. Valk, MEN1 redefined, a clinical comparison of mutation-positive and mutation-negative patients. BMC Med. **14**(1), 182 (2016). https://doi.org/10.1186/s12916-016-0708-1
20. W. Karges, L. Schaaf, H. Dralle, B.O. Boehm, Concepts for screening and diagnostic follow-up in multiple endocrine neoplasia type 1 (MEN1). Exp. Clin. Endocrinol. Diabetes **108**(5), 334–340 (2000)
21. J. Waldmann, V. Fendrich, N. Habbe, D.K. Bartsch, E.P. Slater, P. H. Kann, M. Rothmund, P. Langer, Screening of patients with multiple endocrine neoplasia type 1 (MEN-1): a critical analysis of its value. World J. Surg. **33**(6), 1208–1218 (2009)
22. S. Goswami, B.J. Peipert, I. Helenowski, S.E. Yount, C. Sturgeon, Disease and treatment factors associated with lower quality of life scores in adults with multiple endocrine neoplasia type I. Surgery **162**(6), 1270–1277 (2017). https://doi.org/10.1016/j.surg.2017.07.023
23. C.J. Yates, P.J. Newey, R.V. Thakker, Challenges and controversies in management of pancreatic neuroendocrine tumours in patients with MEN1. Lancet Diabetes Endocrinol. **3**(11), 895–905 (2015). https://doi.org/10.1016/S2213-8587(15)00043-1
24. F.A. Correa, E.C. Farias, L.A. Castroneves, D.M. Lourenco Jr., A. O. Hoff, Quality of life and coping in multiple endocrine neoplasia type 2. J. Endocr. Soc. **3**(6), 1167–1174 (2019). https://doi.org/10.1210/js.2018-00371
25. A. Falchetti, F. Marini, F. Tonelli, M.L. Brandi, Lessons from genes mutated in multiple endocrine neoplasia (MEN) syndromes. Ann. Endocrinol. **66**(3), 195–205 (2005)
26. J. Grey, K. Winter, Patient quality of life and prognosis in multiple endocrine neoplasia type 2. Endocr.-Relat. Cancer **25**(2), T69–T77 (2018). https://doi.org/10.1530/ERC-17-0335
27. B.J. Peipert, S. Goswami, I. Helenowski, S.E. Yount, C. Sturgeon, Financial burden is associated with worse health-related quality of life in adults with multiple endocrine neoplasia type 1. Surgery **162**(6), 1278–1285 (2017). https://doi.org/10.1016/j.surg.2017.07.010
28. M.N. Mongelli, B.J. Peipert, S. Goswami, I. Helenowski, S.E. Yount, C. Sturgeon, Quality of life in multiple endocrine neoplasia type 2A compared with normative and disease populations. Surgery **164**(3), 546–552 (2018). https://doi.org/10.1016/j.surg.2018.04.036
29. B.J. Peipert, S. Goswami, S.E. Yount, C. Sturgeon, Health-related quality of life in MEN1 patients compared with other chronic conditions and the United States general population. Surgery **163**(1), 205–211 (2018). https://doi.org/10.1016/j.surg.2017.04.030
30. R.S. van Leeuwaarde, C.R.C. Pieterman, E.M.A. Bleiker, O.M. Dekkers, A.N. van der Horst-Schrivers, A.R. Hermus, W.W. de Herder, M.L. Drent, P.H. Bisschop, B. Havekes, M.R. Vriens, G. D. Valk, High fear of disease occurrence is associated with low quality of life in patients with multiple endocrine neoplasia type 1: results from the Dutch MEN1 Study Group. J. Clin. Endocrinol. Metab. **103**(6), 2354–2361 (2018). https://doi.org/10.1210/jc.2018-00259
31. N. Frisch, P. Atherton, M.M. Doyle-Waters, M.L.P. MacLeod, A. Mallidou, V. Sheane, J. Ward, J. Woodley, Patient-oriented

research competencies in health (PORCH) for researchers, patients, healthcare providers, and decision-makers: results of a scoping review. Res. Involv. Engagem. **6**, 4 (2020). https://doi.org/10.1186/s40900-020-0180-0
32. J. Hanefeld, T. Powell-Jackson, D. Balabanova, Understanding and measuring quality of care: dealing with complexity. Bull. World Health Organ **95**(5), 368–374 (2017). https://doi.org/10.2471/BLT.16.179309
33. A. Bowling, G. Rowe, N. Lambert, M. Waddington, K.R. Mahtani, C. Kenten, A. Howe, S.A. Francis, The measurement of patients' expectations for health care: a review and psychometric testing of a measure of patients' expectations. Health Technol. Assess. **16**(30), (2012). https://doi.org/10.3310/hta16300
34. L.P. Forsythe, V. Szydlowski, M.H. Murad, S. Ip, Z. Wang, T.A. Elraiyah, R. Fleurence, D.H. Hickam, A systematic review of approaches for engaging patients for research on rare diseases. J. Gen. Intern. Med. **29**(3), 788–800 (2014). https://doi.org/10.1007/s11606-014-2895-9
35. G.R. Polich, Rare disease patient groups as clinical researchers. Drug Discov. Today **17**(3-4), 167–172 (2012). https://doi.org/10.1016/j.drudis.2011.09.020
36. European Commission. EU Survey. 2020. https://ec.europa.eu/eusurvey/home/welcome
37. K.J. Johnson, N.L. Mueller, K. Williams, D.H. Gutmann, Evaluation of participant recruitment methods to a rare disease online registry. Am. J. Med. Genet. Part A **164**(7), 1686–1694 (2014). https://doi.org/10.1002/ajmg.a.36530
38. A.L. Crowe, A.J. McKnight, H. McAneney, Communication needs for individuals with rare diseases within and around the healthcare system of Northern Ireland. Front. Public Health **7** (236), (2019). https://doi.org/10.3389/fpubh.2019.00236
39. M. Tadman, L. Martin, Multiple endocrine neoplasia. in *Advanced Practice in Endocrinology Nursing*, ed. by S. Llahana, C. Follin, C. Yedinak, A. Grossman (Springer International Publishing, Cham, 2019), pp. 1259–1278
40. M. Ruggeri, C. Drago, V. Moramarco, S. Coretti, J. Köppen, M.K. Islam, J. Gibson, R. Busse, J. van Exel, M. Sutton, J.E. Askildsen, C.M. Bond, R.F. Elliott, New professional roles and patient satisfaction: evidence from a European survey along three clinical pathways. Health Policy **122**(10), 1078–1084 (2018). https://doi.org/10.1016/j.healthpol.2018.07.020