



Research Paper

Dutch integrative medicine physicians can improve quality of life of patients with medically unexplained physical symptoms - A cross-sectional observational study



Herman A. van Wietmarschen^{a,*}, Karin van Velthoven^b, Hendrik Jan Hummelen^b, Harry Lamers^b, Rob Elens^b, Ria van Rooijen^b, Bertil de Klyn^b, Martien Zeegers^b, Rob Barthels^b, Jean Pierre Jansen^b, Judith Kocken^b, Roland Lugten^b, Erik-Jan de Rijk^b, Kees den Hertog^b, Alice Robinson^b, Michel de Sonnaville^b, Frans Kusse^b

^a Louis Bolk Institute, Department Nutrition & Health, Kosterijland 3-5, 3981 AJ Bunnik, the Netherlands

^b Medical Doctors Association for Integrative Medicine (AVIG), Koningsweg 234, 3582 GM Utrecht, the Netherlands

ARTICLE INFO

Keywords:

Medically unexplained symptoms
Integrative medicine
General practitioners
Quality of life
Observational study
Case reports

ABSTRACT

Introduction: Integrative Medicine (IM) is a well-established patient centered health care vision which might benefit patients with medically unexplained physical symptoms (MUPS). Case reports were collected from patients with MUPS treated by IM physicians in the Netherlands in order to illustrate IM treatment approaches and demonstrate potential benefits to patients.

Methods: Case reports were classified according to the CARE guidelines from IM physicians who are members of the Medical Doctors Association for Integrative Medicine (AVIG). Data are presented and the quality was assessed using the JBI tool for case reports.

Results: 21 case reports were submitted by 14 IM physicians, most of high quality. Most patients presented with multiple symptoms, of which the most frequently reported were pain ($n = 14$) and fatigue ($n = 7$). The average duration of the symptoms before the first consultation with the IM physician was 36 months (range 1.5 weeks up to 11 years). The average treatment duration was 20 months (range instantaneous up to 10 years). The most frequently used treatment modalities were supplements ($n = 8$), homeopathy ($n = 5$), neural therapy ($n = 4$), dietary advice ($n = 4$). The causality between the IM treatment and the outcome was judged to be very likely in 10 of the case reports, likely in 5 cases, possible in 1 case, unclear in 1 case and could have been the result of natural disease development in 4 of the cases.

Conclusion: The case reports demonstrate that Integrative Medicine provides a highly personalized approach which may be beneficial for MUPS patients.

Introduction

Dutch patients have expressed their need for integrative medicine [1]. One in five Dutch citizens will visit a complementary or integrative medicine care provider within five years [2]. In 2019 a Consortium for Integrative Medicine and Health was established in the Netherlands by 5 Dutch hospitals, a psychiatric institute and a research institute. Nowadays, in 92% of the Dutch hospitals IM is provided, mainly to treat anxiety, restlessness, pain, sleep problems, stress and fatigue [3]. In 2012 the Dutch Medical Doctors Association for Integrative Medicine (AVIG) was founded in order to support IM practice and research in the

Netherlands. The AVIG has 358 members and the number is growing. Most members are medical doctors, some are dentists. All members provide integrative care to their patients. However, further integration of complementary care within institutions has encountered several barriers in the Netherlands, like a lack of knowledge of stakeholders and lack of communication between stakeholders within these institutions [3]. The WHO states the growing importance of traditional and complementary medicine in stimulating a healthy world population and reaching sustainable development goals. In 170 (88%) of the WHO member states the use of traditional or complementary medicine is recognized by the government, policy has been developed, research

* Corresponding author.

E-mail address: h.vanwietmarschen@louisbolk.nl (H.A. van Wietmarschen).

<https://doi.org/10.1016/j.eujim.2022.102140>

Received 9 December 2021; Received in revised form 29 April 2022; Accepted 30 April 2022

Available online 10 May 2022

1876-3820/© 2022 Elsevier GmbH. All rights reserved.

programs are available, and research centres have been established [4]. Integrative Medicine (IM) is currently a well-established part of the healthcare system in the United States, with an Academic Consortium of Integrative Medicine including over 70 academic institutions advancing education, information and research in the field of IM [5]. The National Center for Complementary and Integrative Health (NCCIH) in the US was founded in 1992 and is now part of the National Institutes of Health (NIH) which has spent over 150 million dollar on IM research in 2020 alone.

Integrative Medicine is based on a common set of principles endorsed by the US consortium including: 1) the horizontal relationship between care providers and care receivers, 2) the whole person is taken into account including the mind, spirit, and community, 3) both conventional and alternative methods of treatment are used to facilitate the innate healing response of the body, 4) interventions which are natural and less invasive should be used whenever possible, 5) a variety of scientific methods should be used to evaluate complex interventions, 6) the care provider has a coaching role, the care receiver decides, 7) prevention and health promotion are essential, 8) health care providers should commit themselves to self-exploration and self-development [6, 7].

Conventional medicine offers few treatment options to patients with medically unexplained physical symptoms (MUPS) and seems to have a limited effect [8,9]. Integrative Medicine practitioners using a variety of complementary treatment methods and corresponding worldviews [10] claim to be able to provide answers and improve the quality of life of these patients [11]. However, there is hardly any scientific research available on this topic. A Cochrane review conducted in 2014 on non-pharmacological treatment of MUPS was only able to include studies on psychological interventions, mainly CBT [12]. Only one randomized controlled trial conducted in four London general practices has shown that acupuncture can improve health status and wellbeing [13].

The aim of this cross-sectional observational study was to demonstrate the range of treatment options that IM physicians have to offer patients with medically unexplained physical symptoms (MUPS) and to show the benefits of these treatments. In order to do so, a series of case reports were collected from the members of the AVIG.

Methods

Study design

A cross-sectional observational design was chosen for the presentation of IM physicians approaches for the treatment of MUPS in the Netherlands. The cross-sectional design included the collection of a number of case reports from IM physicians. A Dutch language case-report template was developed based on the CARE-guidelines [14], the HOM-CASE guidelines [15] and the CARE-AAT guidelines [16] (Supplementary file S1). All CARE-guideline topics were included in the template to which explanations were added with references to IM related topics. For instance to the topic 'diagnostic reasoning' the following explanation was added: 'Describe specific diagnostic characteristics and reasoning based on your field of expertise (TCM: syndromes + symptoms, homeopathy: key symptoms, anthroposophy: 3 & 4 foldness, etc.)'. Together with the case-report template a one page checklist was provided in order to check the items covered in the case-report (Supplementary file S2). One researcher was available to answer questions about the case report template and provide feedback on the submitted case reports. In order to improve the quality of the case report the physician was then allowed to provide additional information.

Setting

Case reports were collected from October 2020 till March 2021.

Requests for submission of case reports were issued by the Medical Doctors Association for Integrative Medicine (AVIG) to all of its members via email. The AVIG members are active in all parts of the Netherlands. The first email was sent out in October 2020. The request was repeated in the newsletter of the AVIG and repeated again in another email to the members. A minimum of 15 case reports was aimed for in order to provide an overview of the variety of treatment modalities used by IM physicians and the types of patients they encounter.

Participants

Case reports from patients were included when there were medically unexplained physical symptoms for at least two weeks. Patients suffering from depression, anxiety disorder, dissociative disorder or a personality disorder were excluded. Furthermore, cases were selected in which the physician was able to discern a clear effect of the treatment, and was able to clearly describe this effect or provide objective data concerning this effect. All patients described in the case report gave written informed consent for using and publishing their data. The study did not involve experiments with human subjects and is therefore exempt from ethical approval according to the Dutch Medical Research in Human Subjects Act (WMO). The study is conducted according to the principles set out in the declaration of Helsinki [17].

Outcome evaluation

Outcomes were assessed as objective outcomes per consultation, patient reported outcomes per consultation, physician reported outcomes per consultation, compliance with therapy, therapy tolerability, and adverse events. Special attention was given in the case report template for the reporting of the timing of therapy administrations and reported effects in order to assess the causality of the intervention. Additionally, the IM physicians were asked to provide their own causality assessment of the case.

Data analysis

The data provided by the IM physicians was summarised and extracted into a table format. The quality of the data was assessed by the first author and reviewed by the second and last authors using the JBI checklist for case reports [18]. The causality of the treatment on the outcomes was assessed by the first author and reviewed by the second and last author, using all information available in the case reports and the system of causality assessment described by Kiene et al. [19]. According to the system of causality assessment developed by Kiene the difference between the length of the period of symptoms present and the period of IM treatment and effect is an important factor for causality, a larger period of symptoms with a relatively short treatment period increases the possibility of a causal effect between the outcomes and the treatment.

Results

Participants

In total, 23 case reports were submitted by 15 IM physicians. One physician retracted his two case reports because he objected to publication in an article that would include cases on homeopathy. The remaining 21 case reports were submitted by 14 IM physicians, 3 of whom submitted 3 case reports, 1 of whom 2 case reports and 10 submitted a single case report. Demographics of the 21 patients described in the case reports are presented in Table 1.

Table 2 provides a very brief summary of each of the case reports, presenting the main symptoms, duration of the symptoms, the main interventions, duration of the interventions, the outcomes and the likelihood of a causal relationship between the intervention and the

Table 1
Demographics of the included patients.

Characteristic	Unit	Quantity	
Number of patients	N	21	
Gender			
Male	N (%)	7 (33%)	
Female	N (%)	14 (67%)	
Age			
Mean	Mean (SD)	43 (23)	
Range	Year	10–83	
Symptom duration			
Mean	Month (SD)	36 (38)	
Range	Weeks - years	1.5 wk - 11 yrs	
Therapy duration			
Mean	Month (SD)	20 (36)	
Range	Weeks - years	2 wk - 10 yrs	

outcome assessed by the data analyst. A more comprehensive summary including descriptions of patient histories, clinical conditions, diagnostics, interventions, outcomes, adverse events, patient assessments, physicians assessment and causality assessments is available as Supplementary File S3.

The 21 case reports submitted by AVIG members cover a variety of symptoms and treatment modalities. All authors provided an argumentation for considering the presented symptoms in combination with the patient history as cases of MUPS, at least at the time of the first consultation by the IM physician. Most patients presented with multiple symptoms, of which the most frequently reported were pain ($n = 14$) and fatigue ($n = 7$). The average duration of the symptoms before the first consultation with the IM physician was 36 months. However, there is a large variation in this symptom duration between cases, ranging from 1.5 weeks up to 11 years. The average treatment duration is 20 months, ranging from almost instantaneous up to 10 years. Fig. 1 provides visual presentation of the differences between the period in which symptoms were present before the first IM consultation, and the IM treatment period. This information contributes to the assessment of the causality between the outcomes and the treatment.

The 21 case reports also illustrate the variety of treatment modalities and combinations of treatment modalities that have been used to treat these MUPS cases, the most frequently used are supplements ($n = 8$), homeopathy ($n = 5$), neural therapy ($n = 4$), dietary advice ($n = 4$), acupuncture ($n = 3$), relaxation exercises ($n = 3$), the EMMETT technique (a muscle relaxation technique developed by Ross Emmett) ($n = 3$), and bioresonance ($n = 2$). The reported results at the end of the IM treatment period were very positive in all the cases even though the causality between the intervention and the outcome is not always clear. In 13 cases the symptoms almost entirely disappeared after the IM treatment period, in the other 8 cases there was a clear and substantial improvement in at least one of the symptoms. The overall quality of the case reports was very high, as assessed using the JBI appraisal checklist for case reports (Table 3). Six of the eight items were positively scored for all of the case reports ($n = 21$, 100%). One case report did not provide clear take away lessons ($n = 1$, 5%), and 15 case reports did not report side effects or provided information on side effects ($n = 15$, 71%).

The causality between the IM treatment and the outcome is judged to be very likely in 10 of the case reports, likely in 5 cases, possible in 1 case, unclear in 1 case and could have been the result of natural disease development in 4 of the cases. Striking examples are the case report of a 10 year old boy with frequent vomiting, up to 40 times per day, for three months. A single bioresonance treatment resulted in the complete disappearance of the symptoms within 2 weeks (case 5). In another case of a 52 years old woman with severe hearing impairment of the right ear, neural therapy with a procaine-HCl injection led to immediate return of hearing. Relapses during the following months were successfully treated with procaine injections leading to immediate return of hearing each time (case 15). Finally, the patient was fully cured. In a last example case report, a 15 years old boy suffering from chronic belly ache, headache,

fatigue, and sleep problems for 9 years visited an IM physician and started with an integrated treatment plan consisting of dietary changes, probiotics, exercises, mindfulness, EFT, EMDR and family constellation work which resulted in large reduction of the complaints within 2 months and complete resolving of the symptoms within 14 months (case 6). This case shows that an IM treatment approach can consist of multiple treatment modalities, which reflects current practice in the Netherlands. It shows a rapid effect in 2 months compared with 9 years of symptoms, although we cannot point out which part or combination of parts of the treatment caused the effect.

Discussion

This cross-sectional observational study presents 21 case reports of MUPS patients treated by Integrative Medicine physicians. The case reports demonstrate a variety of options for treating MUPS, even when conventional medicine has nothing more to offer. This is in line with a recent qualitative analysis of 20 German general practitioners dealing with therapeutically indeterminate situations [20]. The study demonstrated an important role for complementary treatments used as active treatment, as beneficial placebo treatment or as relational tools in such situations. The problem for general practitioners dealing with MUPS is often a discrepancy between disease models used by the GP and those used by the patients [21]. An evidence synthesis on general practitioners' perception and management of MUPS pointed out that patients often adhere to a biomedical disease model while GPs see MUPS in the light of a psychosocial disease model, which can lead to frustration and can be a threat to the professional identity of the GPs [22]. Convinced professional users of complementary therapies feel less threatened by the indeterminate situations because they have additional tools available [20].

The variety of case reports illustrates the diversity of medically unexplained physical symptoms. From the causality assessment it is clear that an Integrative Medicine approach can be effective for these patients. In most of the presented cases there is a very likely or likely causal relationship between the IM treatment and the effects. However, it is not clear from the start which type of treatment will work best for which patient. The case reports generally show that Integrative Medicine is a highly personalized whole systems approach in which the treatment is tailored to individual needs and responses. Such whole systems approaches are not focussing on symptoms only, but rather on activating the inherent self-healing mechanisms of the body [23,24].

Limitations

An important limitation of this study is the selection of the case reports, which will probably reflect the best cases of the contributing IM physicians. Therefore there is no way to predict for how many MUPS patients an IM treatment would be beneficial, based on this study. Additionally, the selection of case reports presented in this study might not be representative of the treatments used by IM physicians in the Netherlands.

Conclusion

The study shows the willingness of IM physicians to contribute case reports, and their ability to provide sufficient information in order to write high quality case reports. It also demonstrates that the AVIG and individual IM physicians value scientific research. It appears from this study that MUPS patients presenting with pain and fatigue symptoms can in certain instances be treated successfully by IM physicians. The results of this study can be used to design comparative studies with standardized data collection in the practices of AVIG members in order to gain more insights into promising IM approaches for MUPS patients.

Table 2
Brief summary of the case reports.

Nr	Gender	Age	Main symptoms	Symptom duration	Main therapy type	Therapy duration	Outcome summary	Causality
1	Female	63	Trigeminal neuralgia	5.5 years	Acupuncture (3 sessions), many supplements	10 years	Overall condition improved over time. Many relapses.	Unclear
2	Female	44	Jaw pain, tinnitus, short menstruation cycle	> 5 years (menstruation >23 years)	Acupuncture for jaw (6 sessions), Chinese herbs for menstruation	2 months	Jaw pain decreased over time until gone. Menstruation cycle lengthened to 26/28 days.	Very likely
3	Female	57	Unexplained chronic pain and inflammation in mouth	15 months	Amalgam filling removal, supplements, bioresonance	9 months	Instantaneous 90% symptom reduction	Very likely
4	Male	83	Chronic lower back pain, canal stenosis on MRI	6 years	Autovaccine therapy, vitamin D and B12	1 year	After 8 months pain is gone, canal stenosis is reduced on MRI	Likely
5	Male	10	Frequent vomiting (40 times daily)	3 months	Bioresonance (2 sessions)	2 weeks	Instantaneous disappearance of symptoms after first treatment	Very likely
6	Male	15	Chronic belly ache, headache, fatigue	9 years	Diet, probiotics, exercises, mindfulness, meditation, EFT, EMDR, family constellation	14 months	Symptoms much reduced after two months, then completely gone after 14 months	Very likely
7	Female	37	Hypertonic pelvic floor, incontinence, chronic lower back pain	> 11 years	EMMETT, relaxation exercises, iliopsoas exercise, coaching	3 months	Improvement continence, back pain and more relaxation.	Very likely
8	Female	58	Painful right foot, difficulty walking	> 2 years	EMMETT, relaxation exercises, iliopsoas exercise, coaching (5 sessions)	3.5 months	Symptoms resolved. Symptoms responded directly to the treatment sessions.	Very likely
9	Female	23	Chronic stress, ill feeling, joint pain	several months	High dose vitamin C	Unclear	Symptoms rapidly reduced	Likely
10	Female	13	Fatigue, headache, dizziness, palpitations	5 weeks	Homeopathy	13 months	Symptoms improved slowly over time	Possibly natural healing course
11	Male	74	Neuropathic pain left leg and foot, groin pain left	> 1 year	Homeopathy	> 2 weeks	Groin pain gone in 2 weeks	Likely
12	Female	14	Chronic fatigue, headache, dizziness	16 months	Homeopathy	1 year	Symptoms improved over time. Symptoms repeatedly responded rapidly to taking the treatment after relapsing.	Very likely
13	Female	58	Chronic fatigue, sore muscles	> 4 years	Homeopathy, diet	4 years	Symptoms gone with now and then a relapse.	Possibly natural healing course
14	Male	38	Muscle tension and knots in legs, sleep problems, stress	± 3 years	Homeopathy, supplements, diet	20 months	Symptoms go up and down in response to homeopathy. Rapid improvement after dairy free diet.	Likely with diet
15	Female	52	Hearing impairment right ear	6 weeks	Neural therapy	4–5 months	Repeated immediate return of hearing during injection. Time between relapses increases until cured.	Very likely
16	Female	23	Fatigue in the head after whiplash trauma	3 years 7 months	Neural therapy (13 sessions)	7 months	Strong improvement after 2 months weekly treatment, then slowly declining. Overall much less fatigue in the head.	Very likely
17	Male	NA	Oppression of chest, painful chest muscles and ribs.	1.5 week	Neural therapy (16 sessions)	2 months	Symptoms start declining after 4th treatment. Almost gone after 2 months.	Possibly natural healing course
18	Male	72	Persistent knee pain, leg cramps, numb feet	3 years	Polarization, zell-milieu revitalizing (zmr) program, supplements, neural therapy (5 sessions)	2 months	Great and rapid improvement after 2 weeks. Numbness gone after 2 months	Very likely
19	Female	15	Chronic fatigue, exercise intolerance	4 months	Supplements	7 months	Symptoms and dysbiosis disappeared after 3 months.	Possibly natural healing course
20	Female	60	Bowel symptoms, recurrent UTI, chronic fatigue, sleep problem	many years	Supplements, acupuncture, spiritual healing sessions	10 years	Symptoms were reduced after much trial and error. Spiritual healing (Healing Code, Code of Miracles) had effect.	Possible for spiritual healing
21	Female	55	Tension in body and head, hypertonic pelvic floor	At least several years	Supplements, diet, EMMETT, coaching, relaxation exercises, iliopsoas exercise	5 months	Each treatment reduced tension and improved energy. Posture improved.	Likely

Note: EMMETT = muscle relaxation technique developed by Ross Emmett, EFT = emotional freedom technique, EMDR = Eye Movement Desensitization and Reprocessing, MRI = magnetic resonance imaging, UTI = urinary tract infection.

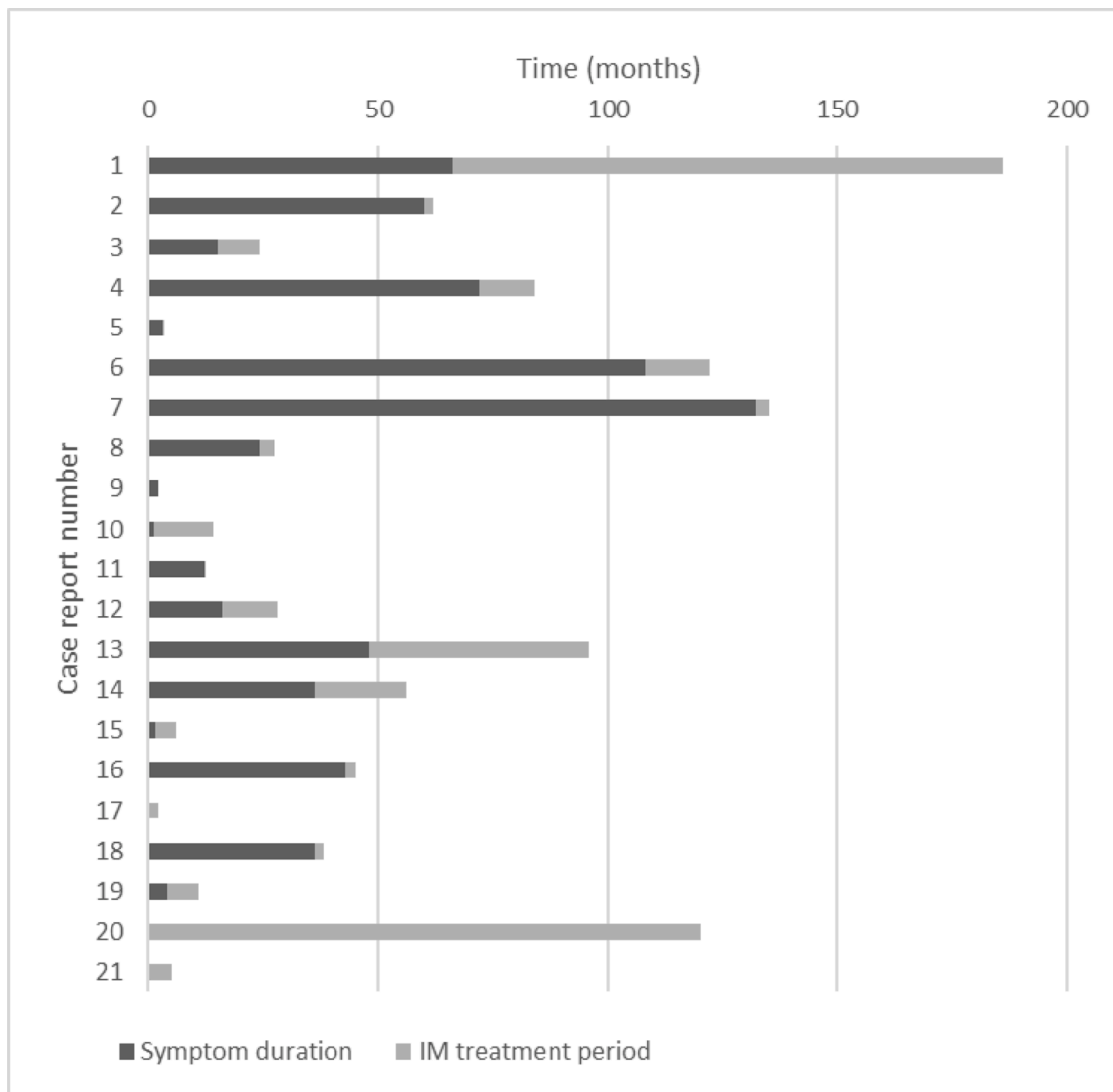


Fig. 1. Overview of the relationship between the duration of symptoms before IM treatment and the duration of the IM treatment for causality assessment.

Table 3
Quality appraisal of the case reports with the JBI checklist for case reports.

JBI item	Case report number																				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Demographics clearly described?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Patients history clearly described?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Clinical condition clearly described?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Diagnostic tests clearly described	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intervention clearly described?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Post-intervention clearly described?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adverse events identified and described?	+	+	+	+	-	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-	-
Are take away lessons provided?	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+

+ indicates a positive answer to the question, - a negative answer.

Author contributions

HAW and FK conceived the project idea. HJH, HL, RE, RR, BK, MZ, RB, JPJ, JK, RL, EJK, KH, AR, MS collected material and wrote the case reports. HAW supported the writing of the case reports and collected the data. Data analysis was performed by HAW. Data interpretation was conducted by HAW, KV, and FK. The manuscript was drafted by HAW. KV and FK reviewed, commented on and approved the final manuscript. All authors read and approved the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

A case report template, case report checklist and a summary of the

case reports are available as supplementary material.

Acknowledgements

The authors thank all health care receivers for their generous consent to use their personal histories and experiences with Integrative Medicine, and time relating this to their IM physician for this study.

Financial support

The study was funded by the Medical Doctors Association for Integrative Medicine (AVIG) and the Hubrechts Research Fund. The funding was used for hiring HAW.

Ethics approval and consent to participate

All health care receivers provided a written informed consent to use their data for the manuscript. Since this is an observational cross-sectional study, no ethics approval is required according to the Dutch Medical Research in Human Subjects Act (WMO).

Data availability and Consent for publication

All health care receivers provided a written informed consent to for publishing their data. All IM physicians collecting and writing the case reports provided written informed consent for publishing the data.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.eujim.2022.102140](https://doi.org/10.1016/j.eujim.2022.102140).

References

- [1] M. Jong, L. van de Vijver, M. Busch, J. Fritsma, R. Seldenrijk, Integration of complementary and alternative medicine in primary care: what do patients want? *Patient Educ. Couns.* 89 (2012) 417–422, <https://doi.org/10.1016/j.pec.2012.08.013>.
- [2] R. Kloosterman, *Alternatieve geneeswijzen : contact en opvattingen samenwerking*, 2019.
- [3] M.C. Jong, M. Busch, E.W. Baars, Integrative medicine in Dutch curative and long-term healthcare centres: mapping the field, *Eur. J. Integr. Med.* 28 (2019) 14–19, <https://doi.org/10.1016/j.eujim.2019.04.003>.
- [4] WHO, *Who global report on traditional and complementary medicine 2019*, Geneva, 2019.
- [5] B. Horrigan, S. Lewis, M. Donald Abrams, P. for the B.C. Constance Pechura, *Integrative Medicine in America: how Integrative Medicine Is Being Practiced in Clinical Centers Across the United States*, Bravewell Collab (2012) 1–116, <https://doi.org/10.7453/gahmj.2012.1.3.006>.
- [6] V. Maizes, D. Rakel, C. Niemiec, *Integrative Medicine and Patient-Centered Care*, *Explor. J. Sci. Heal.* 5 (2009) 277–289, <https://doi.org/10.1016/j.explore.2009.06.008>.
- [7] B. Barrett, L. Marchand, J. Scheder, M.B. Plane, R. Maberry, D. Appelbaum, D. Rakel, D. Rabago, *Themes of Holism, Empowerment, Access, and Legitimacy Define Complementary, Alternative, and Integrative Medicine in Relation to Conventional Biomedicine*, *J. Altern. Complement. Med.* 9 (2003) 937–947, <https://doi.org/10.1089/107555303771952271>.
- [8] M. den Boeft, D. Huisman, L.K. Morton, P. Lucassen, J.C. van der Wouden, M. J. Westerman, H.E. van der Horst, C.D. Burton, *Negotiating explanations: doctor-patient communication with patients with medically unexplained symptoms-A qualitative analysis*, *Fam. Pract.* 34 (2017) 107–113, <https://doi.org/10.1093/fampra/cmw113>.
- [9] O.T. Hartman, B.D. van den Berg, *NHG-Standaard Somatisch onvoldoende verklaarde lichamelijke klachten (SOLK)-pagina 1 NHG-Standaard Somatisch onvoldoende verklaarde lichamelijke klachten (SOLK) (M102)*, (2013).
- [10] A. Hedlund-de Witt, J. de Boer, J.J. Boerema, *Exploring inner and outer worlds: a quantitative study of worldviews, environmental attitudes, and sustainable lifestyles*, *J. Environ. Psychol.* 37 (2014) 40–54, <https://doi.org/10.1016/j.jenvp.2013.11.005>.
- [11] A.L. Kirkengen, T.-J. Ekeland, L. Getz, I. Hetlevik, E. Schei, E. Ulvestad, A. J. Vetlesen, *Medicine's perception of reality - a split picture: critical reflections on apparent anomalies within the biomedical theory of science*, *J. Eval. Clin. Pract.* (2015), <https://doi.org/10.1111/jep.12369> n/a-n/a.
- [12] N. van Dessel, M. den Boeft, J. van der Wouden, M. Kleinstäuber, S. Leone, B. Terluin, M. Numans, H. van der Horst, H. van Marwijk, *Non-pharmacological interventions for somatoform disorders and medically unexplained physical symptoms (MUPS) in adults*, *Cochrane Database Syst. Rev.* (2014), <https://doi.org/10.1002/14651858.CD011142.pub2.www.cochranelibrary.com>.
- [13] C. Paterson, R. Taylor, P. Griffiths, P. Britten, S. Rugg, J. Bridges, B. McCallum, G. Kite, *Acupuncture for "frequent attenders" with medically unexplained symptoms*, *Br. J. Gen. Pract.* 61 (2011) 494, <https://doi.org/10.3399/bjgp11x588330>.
- [14] J.J. Gagnier, G. Kienle, D.G. Altman, D. Moher, H. Sox, D. Riley, A. Allaire, J. Aronson, J. Carpenter, J. Gagnier, P. Hanaway, C. Hayes, D. Jones, M. Kaszkin-Bettag, M. Kidd, H. Kiene, G. Kienle, B. Kligler, L. Knutson, C. Koch, K. Milgate, M. Mittelman, H. Oltean, G. Plotnikoff, R.A. Rison, A. Sethi, L. Shamseer, R. Smith, P. Tugwell, *The CARE guidelines: consensus-based clinical case report guideline development*, *J. Diet. Suppl.* 10 (2013) 381–390, <https://doi.org/10.3109/19390211.2013.830679>.
- [15] R.A. van Haselen, *Homeopathic clinical case reports: development of a supplement (HOM-CASE) to the CARE clinical case reporting guideline*, *Complement. Ther. Med.* 25 (2016) 78–85, <https://doi.org/10.1016/j.ctim.2015.12.019>.
- [16] A. Abbing, A. Ponstein, G. Kienle, H. Gruber, E. Baars, *The CARE-AAT Guideline: development and testing of a consensus-based guideline for case reports in anthroposophic art therapy*, *Int. J. Art Ther. Inscapc.* 21 (2016) 46–55, <https://doi.org/10.1080/17454832.2016.1170054>.
- [17] *World Medical Association, World Medical Association Declaration of Helsinki*, *JAMA* 310 (2013) 2191–2194, <https://doi.org/10.4324/9781315572093-15>.
- [18] S. Moola, Z. Munn, C. Tufanaru, E. Aromataris, K. Sears, R. Sfetcu, M. Currie, R. Qureshi, P. Mattis, K. Lisy, P.-F. Mu, *Systematic reviews of etiology and risk*, in: E. Aromataris, Z. Munn (Eds.), *JBI Man, Evid. Synth*, 2020.
- [19] H. Kiene, H.J. Hamre, G.S. Kienle, D. Moher, H. Sox, D. Riley, *Support of Clinical Case Reports: a System of Causality Assessment*, *Glob. Adv. Heal. Med* 2 (2013) 64–75, <https://doi.org/10.7453/gahmj.2012.061>.
- [20] A. Ostermaier, N. Barth, A. Schneider, K. Linde, *On the edges of medicine - A qualitative study on the function of complementary, alternative, and non-specific therapies in handling therapeutically indeterminate situations*, *BMC Fam. Pract.* 20 (2019) 1–10, <https://doi.org/10.1186/s12875-019-0945-4>.
- [21] T. Woivalin, G. Krantz, T. Mäntyranta, K.C. Ringsberg, *Medically unexplained symptoms: perceptions of physicians in primary health care*, *Fam. Pract.* 21 (2004) 199–203, <https://doi.org/10.1093/fampra/cmh217>.
- [22] M.L. Johansen, M.B. Risor, *What is the problem with medically unexplained symptoms for GPs? A meta-synthesis of qualitative studies*, *Patient Educ. Couns.* 100 (2017) 647–654, <https://doi.org/10.1016/j.pec.2016.11.015>.
- [23] H.A. van Wietmarschen, H.M. Wortelboer, J. van der Greef, *Grip on health: a complex systems approach to transform health care*, *J. Eval. Clin. Pract.* (2016) 1–9, <https://doi.org/10.1111/jep.12679>.
- [24] P.J. Mills, S. Patel, T. Barsotti, C.T. Peterson, D. Chopra, *Advancing research on traditional whole systems medicine approaches*, *J. Evidence-Based Complement. Altern. Med.* 22 (2017) 527–530, <https://doi.org/10.1177/2156587217745408>.