

Incidence and prevalence of vitreomacular traction with and without macular hole in Germany

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Purpose: Symptomatic vitreomacular adhesion (sVMA) comprises vitreomacular traction (VMT) and stage 1 and 2 full-thickness macular holes (MHs) associated with vitreomacular adhesion (VMA). We aimed to estimate the incidence and prevalence of sVMA in Germany.

Materials and methods: A systematic literature review was conducted to identify the incidence and prevalence of sVMA based on international epidemiologic studies, weighted for study size and then averaged across eligible studies. A second systematic review aimed to estimate the proportion of vitrectomy undertaken for sVMA in Germany. This was combined with the reported number of vitrectomies in Germany in 2016 to estimate the number of patients undergoing vitrectomy for sVMA.

Results: The prevalence of sVMA is 1,365 per 100,000 population, with an incidence of 6.96 per 100,000 per year. For Germany, this translates to 1,119,300 cases, with 5,700 new cases reported annually. Analyzing the national hospital statistics, ~2,300 patients undergo vitrectomy due to sVMA in Germany each year, of which about 1,700 patients have VMT.

Conclusion: Incidence figures, driven by patients presenting to clinic, are much lower than expected based on population-based studies, suggesting that many patients with sVMA exist outside of the clinic system.

Keywords: epidemiology, vitreous body, vitreous pathology, vitreous adhesion, vitreous detachment, pars plana vitrectomy

Introduction

As part of normal aging, the vitreous body liquefies and usually starts to separate from the posterior retina, described as posterior vitreous detachment. Incomplete separation at the macula is described as vitreomacular adhesion (VMA), which is not, in itself, pathological and is, by definition, not associated with morphological alterations of the retina or functional loss. In contrast, if residual, focal, vitreomacular tractional (VMT) forces lead to a distortion of retinal tissue, visual symptoms may occur. This condition is described as VMT (syndrome). In the course of VMT, the development of a full-thickness macular hole (MH) may be observed. In the literature, VMT, with or without MH, is often referred to as symptomatic VMA (sVMA).

Structural changes are usually best seen using optical coherence tomography (OCT) and are characterized by retinal distortion, intraretinal cysts, and foveal elevation. Full-thickness MHs may retain vitreous traction, or this may subsequently pull free. Both VMT and MH may resolve spontaneously, although this becomes increasingly unlikely with increasing size or longer duration of an MH.¹

Symptoms of sVMA typically include metamorphopsia and decreased distance and reading visual acuity,² although some patients describe significant symptoms despite relatively well-preserved retinal structures. The indication of treatment of sVMA

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is usually based on the patients' complaints and function, and includes watchful waiting in less-pronounced cases, an intravitreal injection of a vitreolytic agent (ocriplasmin), or pars plana vitrectomy (PPV).^{1,3}

While the epidemiology of MHs is relatively well documented, this is not always broken down by MH stage or the presence or absence of vitreous adhesion. Therefore, combined with incomplete epidemiological data on VMT, the overall epidemiological burden of sVMA is unclear. To address this uncertainty, Jackson et al completed a systematic review regarding the epidemiology of sVMA,⁴ which was published 5 years ago. One may hypothesize that since then, figures may have changed due to an aging population and, even more important, higher-resolution OCT imaging being available. Based on the developments of high-resolution imaging, the staging of these conditions was revisited and new classification systems for sVMA and MHs have been suggested.^{1,2,5} However, for the present investigation, we used the MH classification published by the American Academy of Ophthalmology (AAO).¹ Given this background, we aimed to update Jackson's analysis using international published data and then combine this with German vitrectomy data in order to estimate the burden of sVMA in Germany.

Materials and methods

Two systematic literature searches were conducted using the EMBASE and Medline databases and the Ovid interface. The first literature search targeted all eligible epidemiologic studies concerned with VMT and idiopathic MHs. The second collected all available data on MH staging and surgery in Germany. For the number of vitrectomies due to MH, we analyzed hospital data from the German national hospital reimbursement data.⁶

Search for epidemiologic studies on VMT

In the first search, we used the following search terms in all search fields: vitreomacular traction, vitreoretinal traction, VMT, VMTS (vitreomacular traction syndrome), vitreomacular adhesion, vitreoretinal adhesion, VMA, vitreous AND macula AND separation, vitreous detachment, retinal detachment, macular detachment, macular hole, MH, retinal Hole, full-thickness macular hole, macular foramen and FTMH.

To filter for epidemiologic literature, we used the term "Epidemiology[MeSH:NoExp] OR Incidence[Title/abstract] OR Prevalence[Title/abstract] OR Epidemiology[Title/abstract]" as proposed by Orphan.net.⁷ The details of the search strategies are shown in Table S1.

The search was conducted on February 19, 2018, by JM and AN, who independently sorted the articles and extracted the data. Differences were solved by discussion. To be included in the study, articles had to meet the inclusion and exclusion criteria listed in Table 1.

MH stages in German vitrectomy patients

In the second search, we applied the following disease terms in all search fields: vitreomacular traction, vitreoretinal traction, VMT, VMTS, vitreomacular adhesion, vitreoretinal adhesion, macular hole, MH, Retinal Hole, full-thickness macular hole, macular foramen and FTMH. Defining the intervention, we used the terms "vitrectomy OR PPV OR pars plana OR surgery OR operation" in all fields and combined both searches using the AND operator.

The resulting set of articles was condensed by searching for the term "German" in all search fields. The search was conducted on February 19, 2018, by JM and AN, who independently selected the articles and extracted the data. Differences were resolved by discussion. The articles were

Table 1 Exclusion and inclusion criteria for epidemiologic papers in VMT and MH

Criterion	Inclusion criteria	Exclusion criteria
Population	I1: Adult patients with VMT	E1: No adult patients with VMT
Indication	I2: Treatment of VMT in adults, also together with a macular hole equal to or smaller than 400 μm	E2: No treatment of VMT in adults, also together with a macular hole equal to or smaller than 400 μm
End points	I3: Epidemiologic measures <ul style="list-style-type: none"> • Incidence • Prevalence 	E3: No epidemiologic measure
Type of publication	I4: Full-text publications	E4: Publications, where no full text is available (eg, conference abstracts, letters)
Type of study	I5: Epidemiologic survey	E5: Case studies, small case series, or studies not representative for the respective population
Date of publication	I6: After 1996	E6: Before 1996
Language	I7: German or English	E7: Other languages

Abbreviations: MH, macular hole; VMT, vitreomacular traction.

Table 2 Exclusion and inclusion criteria for German studies on MH staging among the German patient population

Criterion	Inclusion criterion	Exclusion criterion
Population	I1: Adult patients for vitrectomy	E1: No adult patients for vitrectomy
Intervention	I2: Vitrectomy	E2: No vitrectomy
Staging	I3: Macular hole staging (after Gass/AAO)	E3: No macular hole staging (after Gass/AAO)
Type of publication	I4: Full-text publications	E4: Publications, where no full-text is available (eg, conference abstracts, letters)
Type of study	I5: Epidemiologic survey	E5: Case studies, small case series, or studies not representative for the respective population
Language	I7: German or English	E7: Other languages
Sample size	I8: Patient number ≥ 5	E8: Patient number < 5
Nationality	I9: German patients	E9: No German patients

Abbreviations: AAO, American Academy of Ophthalmology; MH, macular hole.

sorted based on the inclusion and exclusion criteria listed in Table 2. Search strategies are shown in detail in Table S2.

Number of vitrectomies due to an MH in Germany

We determined the number of PPVs in Germany in 2016 for a VMT using data from the Institut für das Entgeltssystem im Krankenhaus (InEK), the institute that facilitates reimbursement to hospitals. InEK collects all codes used by hospitals for billing of medical services.⁶ The codes used were ICD-10, Diagnosis Related Groups (DRG), and Operationen und Prozedurenschlüssel (OPS), all version 2016.

We filtered the data set for patients with the DRG codes C03A, C03B, or C03C indicating a retinal surgery. Two subsets were created using either the ICD-10 codes for macular pathology, H35.3 and H35.8, that include the diagnoses of VMT and MH, or the OPS codes for retinal surgery including macular manipulation 5-158.0, 5-158.1, 5-158.2, 5-158.4, 5-158.x, 5-158.y. The OPS codes included all relevant PPVs.⁸ Finally, we searched for patient numbers emerging in both DRG code subsets, created using either the ICD-10 codes or the OPS codes. Those patients matching both criteria (diagnosis defined by ICD and procedure defined by OPS) were assumed to have undergone vitrectomy due to an MH, VMT, and/or epiretinal membrane as well as some less-frequent macular diseases. Distribution of MH stages from the systematic literature research was applied to derive numbers for stage 1 and 2 MH.

Results

VMT prevalence and incidence in population-based studies

The systematic literature search for international epidemiologic studies resulted in 3,039 articles. This included

1,409 duplicates that were identified by review of the title and abstract and then removed. The abstract and title search resulted in 43 articles for full-text screening, of which 12 met the eligibility and were included (Table 1). Figure 1 shows the flowchart of the systematic literature search.

Seven publications reported epidemiologic data on VMT and five on MH. Study details are shown in Table 3, listing design, population, sample size, diagnostic methods, and epidemiologic measures. With the exception of three studies,^{9–11} all used OCT to diagnose VMT or MH. In most studies, the MH stage was not reported according to the current AAO classification.¹

All studies included quite large population samples, with varying estimates of VMT prevalence that are summarized in Table 3. The incidence rate was estimated in only one study.⁴ For MH, both rates were estimated by at least three publications (Table 1). From the given rates, we calculated the arithmetic average (Table 3).

For VMT, we calculated from seven studies with a total of 18,859 participants (age range: 32–90 years) an average prevalence of 1.263 cases per 100,000. The incidence rate was reported by only one study with 0.56 cases per 100,000.⁴ Averaging the data of five studies with a total of 123,621 participants (age range: 26–90 years), we calculated an average prevalence for MH of 141 cases per 100,000 and an average annual incidence of 8.8 cases per 100,000.

We then aimed to refine these incidence and prevalence figures to consider just the subpopulation which had sVMA, namely, VMT with or without MH (Table 4). All patients with a diagnosis of VMT were included, while those patients diagnosed with an MH only (72.8%) had a concomitant VMT according to Jackson's review of the literature.⁴ Therefore, the incidence and prevalence rates for MH were reduced to 72.8% of their reported values in Table 4 to capture only

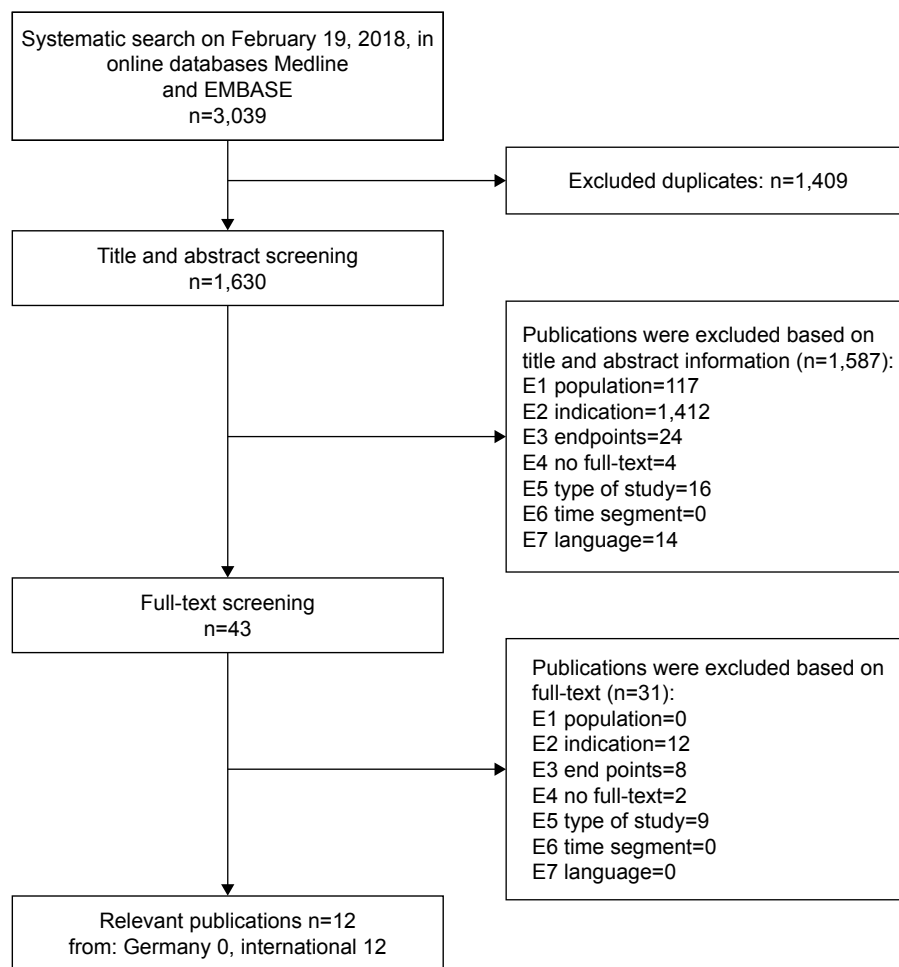


Figure 1 Flowchart of the systematic literature search on international epidemiology papers for VMT.
Abbreviation: VMT, vitreomacular traction.

those MHs with coexisting VMT. The resulting prevalence rate, including all cases of VMT plus all MH cases with coexisting VMT, was 1.365 cases per 100,000 inhabitants with an incidence rate of 6.96 new cases per 100,000 inhabitants per year. Applied to the German population of roughly 82 million, every year, about 5,700 new cases of sVMA would be observed. From the literature, a prevalent pool of 1,119,300 patients is calculated.

MH stages in German vitrectomy patients

The literature search about MH stage rates in Germany resulted in 719 hits containing 159 duplicates. From these, 31 articles (Table 3) were included. Figure 2 shows the flowchart of the systematic literature search.

To estimate the surgical numbers for Germany based on real-world clinical data, we first made a literature search to determine the MH stage distribution of patients in Germany who underwent a PPV. Included studies are listed in Table 5, indicating sample size and staging distribution.

For evaluation, we pooled the patients of stages 3 and 4 and calculated the weighted average.

About 77% of all patients receiving a PPV for MHs in Germany had a stage 3 or 4 MH. Therefore, 23% had a stage 1 or 2 MH, including VMT.

Estimation of German VMT patients based on hospital surgery statistics

According to the INEK data, 52,223 patients underwent retinal surgery in Germany in 2016 and 34,314 of these underwent a PPV based on OPS codes. Of the 52,223 patients, about 15,878 had ICD-10 codes H35.3 or H35.8, indicating any macular changes, including VMT and MH, but also including patients with surgery for other macular changes such as epiretinal membrane. Selecting patients in the overlap of the ICD-10 and OPS subgroups resulted in a sample of 9,941 patients. This group most likely included patients who underwent a PPV for MH or VMT, but due to nonspecific codes with the ICD-10 and OPS, it is likely that it also

Table 3 Summary of epidemiologic studies on vitreomacular traction and MH, giving the average weighted rates of prevalence and incidence from all studies

No	Reference	Design	Population, age span	Diagnostic methods	Prevalence rate (bold: normalized to 100,000 inhabitants)	Incidence rate (bold: normalized to 100,000 inhabitants)	Remarks
VMT							
1	Jacob et al, 2016 ¹²	Cross-sectional study, 2013	N=481, 34–66 years Randomly chosen adult Belgians in a public hospital during open door day	Cirrus 5000 OCT	VMT with retinal distortion 1,170, VMT with retinal cysts 390 VMT prevalence for age <50 years=0; for age >50 years: VMT "grade 1" (fovea distortion)=1.17% (3 eyes), VMT "grade 2" (with pseudocysts)=0.39% (1 eye)	–	
2	Jackson et al, 2013 ⁴	Retrospective data analysis 2002–2010	N=8,741, 32.4–89.2 years 11,618 vitreoretinal operations of 9,619 eyes (8,741 patients) from 27 hospitals (age 32.4–89.2 years, median: 65)	Intraoperative	(22.5^a – not included in the average) 1.5% of 11,618 operations (n=174), that is, 1.6% of eyes (n=167) were due to a VMT	0.56^a VMT cases	
3	Liesenborghs et al, 2018 ²¹	Prospective observational cohort study 2010–2013	N=2,660, 40–75 years Randomly chosen subjects	OCT	1,900 VMT retinal changes Of 2,660 subjects, 183 (6.9%) were diagnosed with a VMT. Of these, 51 (1.9%) had a VMT with retinal changes (elevations or cysts) No MHs were diagnosed; MH prevalence was 0%	–	"VMT" without retinal changes could be "VMA". Symptoms were not specified
4	McKibbin et al, 2017 ²² "UK Biobank"	Database study. Patients with VRIA were identified in the British Biobank	2,090, 40–69 years Of 133,668 registered subjects, 8,359 had visual impairments, of which 2,090 were included in the study. Mean age was 61 years	OCT (Topcon 1000), Funduscopy	870 VMT cases with visual impairment For the 1,684 patients with monocular visual impairment, the VMT prevalence at the fovea was 0.87% (n=14); extrafoveal "VMT" was 0.62% (n=10) For controls without visual impairment (n=472), the VMT prevalence for both VMT types was 0.65% (n=4), respectively	–	Small difference in the VMT frequency for eyes with and without impairment
5	Meuer et al, 2015 ¹³ "Beaver Dam" Study 20-year Update (Beaver Dam)	Prospective cohort study 2008–2010	N=1,540, >43 years	Spectral-domain OCT	1,400 VMT cases VMT prevalence was 1.6% (28 eyes of 24 subjects from 1,540 participants)	–	VMA had a higher prevalence with 26% (551 eyes of 400 participants) After age adjustment, no difference between the sexes

(Continued)

Table 3 (Continued)

No	Reference	Design	Population, age span	Diagnostic methods	Prevalence rate (bold: normalized to 100,000 inhabitants)	Incidence rate (bold: normalized to 100,000 inhabitants)	Remarks
6	Rodman et al, 2017 ¹⁴	Prospective, cross-sectional study 2012–2014	1,090, 40–89 years Patients from 14 centers. Included were patients who attended for routine eye examination Age >40 years, average: 56.2±9.7	Spectral-domain OCT	1,100 VMT cases Prevalence of VMT 1.1% of all eyes (n=21 of 1,950 eyes)	–	VMA more frequent with 38.8% (756 eyes)
7	Zapata et al, 2017 ²³	Cross-sectional study 2015–2016	2,257, age 45–90 years Participants at 17 centers (4,490 eyes), age >45 years. Average: 59.5 years	Spectral-domain OCT or swept-source OCT	600 VMT cases VMT prevalence 0.6% (n=14 of all participants)	–	VMA more frequent with 29.3% (1,317 eyes)
Total participants			18,859	Arithmetic average^b	1,263	0.56^a	
MH							
8	Darian-Smith et al, 2016 ⁴⁴	Retrospective consecutive case series of a surgeon 2005–2011	136, age 26–90 years stage 2–4 MH at one Australian (Tasmanian) center (age: 69±8.8)	OCT	–	4.05 Incidence for idiopathic, FTMH	The analysis covered all cases of the complete Tasmanian population
9	la Cour and Friis, 2002 ¹⁰ Beaver Dam Study cp. Meuer et al, 2015	Prospective cohort study (Beaver Dam) cp. Meuer et al, 2015	4,802, 43–84 years Beaver Dam Study data Patients >42 years Span 43–84 years	Funduscopy	140 cases Prevalence MH 0.3% – age-normalized prevalence 0.14%	30 cases Incidence MH 300 cases per 1 million per year	Beaver Dam 10-year incidence 0.7% (R Klein, personal communication)
10	Mccannel et al, 2009 ²⁵	Retrospective chart review 1992–2002	106,470, 48–90 years	Clinic, sometimes OCT		7.8 cases Incidence of idiopathic MH in Olmstead, Minnesota	
11	Sen et al, 2008 ⁹	Cross-sectional study, 2008	7,774, >40 years Average: 53.93±10.41 years	Funduscopy and fundus photography	170 cases Prevalence MH 0.17% (=13 subjects)	–	
12	Wang et al, 2006 ¹¹ ("Beijing" Study)	Cross-sectional study 2006	4,439, >40 years representative participants aged >40 years (8,653 eyes), age 55.9±10.4 years, one center	Fundus photography	Prevalence of FTMH was 0.09%±3.04% eyes (8 eyes of 7 patients), 95% CI=0.03%–0.16%	–	
Total participants			123,621	Arithmetic average^b	141	8.8	

Notes: ^aOnly cases treated with vitrectomy. Calculation from Simpson and Jackson;²⁶ 2.1% of all vitrectomies due to VMT. Total vitrectomies=16,500 per year in Great Britain with 62.3 Mio inhabitants results in 0.56 cases per 100,000. The publication estimate for VMT including MH prevalence was 1,574 cases and the incidence was 31.3 cases per 100,000 inhabitants. ^bWeighted average, that is, average of all groups adjusted to the size of the study population. Larger studies impact the average more.

Abbreviations: FTMH, full-thickness macular hole; MH, macular hole; OCT, optical coherence tomography; VMA, vitreomacular adhesion; VMT, vitreomacular traction; VRIA, vitreoretinal interface abnormalities.

Table 4 Summary of calculation of the prevalence and incidence of VMT from the literature estimates for VMT and MH

Staging	Population applicable (%)	VMT prevalence (per 100,000 inhabitants) ^a	VMT incidence (per 100,000 inhabitants) ^a
VMT: All stages	100	1,263	0.56
MHs	72.8	102	6.4
Sum		1,365	6.96

Note: ^aCalculated from weighted values found in the studies identified in the systematic literature search.

Abbreviations: MH, macular hole; VMT, vitreomacular traction.

included patients with other macular diseases, in particular, epiretinal membrane.

Applying the stage distribution given in the literature (Table 5) to these 9,941 patients, 7,655 patients had a stage 3 or 4 MH and 2,287 patients had an sVMA, that is, stage 1 or 2 MH and/or a VMT. Considering that not all MHs show concomitant VMT, only 72.8% of patients with MH had concomitant VMT,⁴ the numbers for stage 1 or 2 MHs and a VMT reduced to 1,665 vitrectomies for patients with VMT or MH stages 1 or 2 with VMT in Germany.

Discussion

In the present work, we estimated the incidence and prevalence of VMT, with and without MH, based on 12 large international studies. We found a prevalence of 1,365 cases per 100,000 population and an incidence rate of 6.96 new cases per 100,000 population per year.

There is an apparent discrepancy between the incidence and prevalence rates, in that the prevalence is more than expected based on incident cases. There may be several reasons for this difference. First, the rate of spontaneous

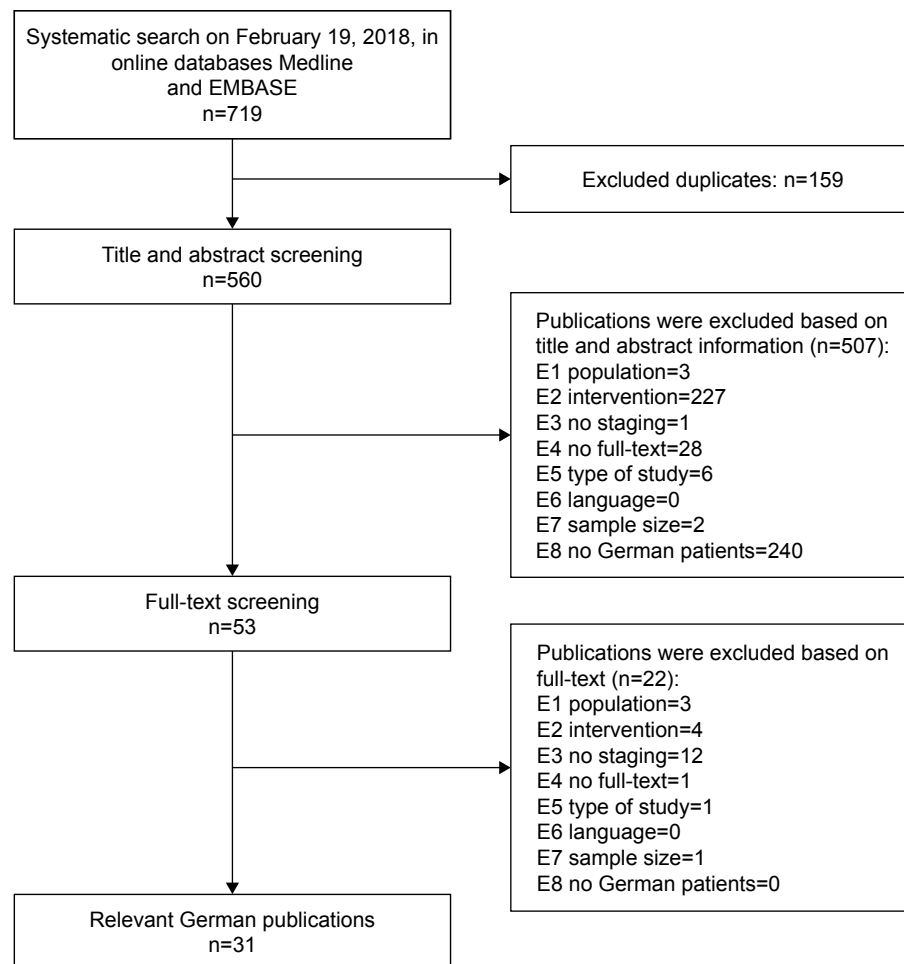


Figure 2 Flowchart of the systematic literature search on German papers staging MH patients undergoing a vitrectomy.

Abbreviation: MH, macular hole.

Table 5 German studies on staging MH patients undergoing PPV surgery

No	Author, year	Study design	Patient number	Stage distribution in %				Patients in % MH >400 µm
				I	II	III	IV	Stages III and IV
1	Beutel et al, 2007 ²⁷	Randomized clinical trial	40	0.0	5.0	77.5	17.5	95.0
2	Bopp et al, 1997 ²⁸	Prospective study	50	2.0	22.0	60.0	16.0	76.0
3	Brockmann et al, 2011 ²⁹	Prospective study	25	12.0	24.0	36.0	28.0	64.0
4	Brockmann et al, 2013 ³⁰	Retrospective study	160	0.0	6.9	37.5	55.6	93.1
5	Eckardt et al, 2008 ³¹	Prospective study	33	0.0	45.5	27.3	27.3	54.6
6	Eckardt and Eckardt, 1995 ³²	Prospective study	37	5.4	48.6	35.1	10.8	45.9
7	Engelmann et al, 2015 ³³	Retrospective study	45	0.0	6.7	13.3	80.0	93.3
8	Faude et al, 1997 ³⁴	Prospective study	19	0.0	21.1	57.9	21.1	79.0
9	Gass et al, 2003 ³⁵	Retrospective cohort study	18	5.6	0.0	88.9	5.6	94.5
			21	4.8	0.0	71.4	23.8	95.2
			17	5.9	0.0	82.4	11.8	94.2
10	Gehring et al, 1999 ³⁶	Randomized clinical trial	19	0.0	21.1	47.4	31.6	79.0
11	Göbel et al, 2000 ³⁷	Retrospective cohort study	36	0.0	33.3	50.0	16.7	66.7
12	Göbel and Guthoff, 2010 ³⁸	Retrospective cohort study	10	0.0	10	70.0	20.0	90.0
13	Hager et al, 2005 ³⁹	Retrospective cohort study	137	0.0	0.0	100.0		100.0
14	Haritoglou et al, 2001 ⁴⁰	Prospective cohort study	105	0.0	7.6	78.1	14.3	92.4
15	Haritoglou et al, 2006 ⁴¹	Prospective study	14	0.0	0.0	100		100.0
16	Hillenkamp et al, 2007 ⁴²	Retrospective cohort study	28	0.0	28.6	71.4		71.4
17	Hoerauf et al, 2001 ⁴³	Prospective study	44	0.0	27.3	47.7	25.0	72.7
18	Jenisch et al, 2017 ⁴⁴	Retrospective study	225	0.0	52.0	32.0	16.0	48.0
19	Jordan et al, 2012 ⁴⁵	Prospective study	26	15.4	23.1	38.5	23.1	61.6
20	Krömer et al, 2004 ⁴⁶	Prospective study	20	0.0	0.0	100.0	0.0	100.0
21	Kristin et al, 2001 ⁴⁷	Prospective study	78	0.0	7.7	76.9	15.4	92.3
22	Kube et al, 2002 ⁴⁸	Retrospective cohort study	107	0.0	63.6	33.6	2.8	36.4
23	Mayer et al, 2014 ⁴⁹	Prospective study	16	0.0	0.0	37.5	62.5	100.0
24	Meyer et al, 2008 ⁵⁰	Prospective study	91	0.0	12.1	56.1	31.8	87.9
25	Rüfer et al, 2007 ⁵¹	Retrospective cohort study	61	0.0	11.5	77.0	11.5	88.5
26	Remy et al, 2008 ⁵²	Retrospective cohort study	14	0.0	28.6	35.7	35.7	71.4
27	Schrader and Schrenker, 1999 ⁵³	Prospective study	39	0.0	20.5	79.5		79.5
28	Schumann et al, 2007 ⁵⁴	Retrospective cohort study	96	0.0	0.0	80.2	19.8	100.0
29	Wirbelauer et al, 2011 ⁵⁵	Prospective study	21	0.0	25.0	75.0	0.0	75.0
30	Wirbelauer et al, 2016 ⁵⁶	Prospective study	47	0.0	36.2	63.8	0.0	63.8
31	Wolf et al, 2003 ⁵⁷	Retrospective cohort study	37	0.0	35.1	56.8	8.1	64.9

Notes: Proportion of vitrectomized patients with an MH at stages 3 and 4, arithmetic average=79.6%. Proportion of vitrectomized patients with an MH at stages 3 and 4, weighted average=77.5%.

Abbreviations: MH, macular hole; PPV, pars plana vitrectomy.

resolution of VMT (with or without MH) could be higher than previously assumed, and thus, only a small proportion of lesions that exist in the population-based studies (which drives our prevalence rates) progress to eye clinics/hospitals (which drives our incidence rates). This is possible as our understanding of the natural history of VMT and MH is largely based on clinical data, whereas the natural history of those outside of a clinic/hospital environment may differ.

The use of OCT may also enable us to detect lesions much earlier than in previous studies, and earlier lesions might be more likely to resolve. Perhaps, the most likely explanation is that population-based studies may pick up asymptomatic cases that do not progress to intervention, unlike studies based on patients presenting to clinic or surgery.¹²⁻¹⁴ More epidemiologic studies are needed to determine the sVMA incidence rates.¹⁵

Given the existing uncertainties of results from the systematic literature review, we aimed to further validate our results with other data sources: As one validation step, we considered the number of MH patients predicted by the literature with an incidence rate for MHs of 8.8 patients per 100,000 adult inhabitants (Table 1), suggesting ~7,200 new MH patients for Germany per year. This is in good accordance with 2016 German vitrectomy statistics, which suggest that 9,941 patients received surgery for MH or VMT – a figure that potentially also includes patients with other macular diseases, in particular, epiretinal membrane.

As another validation step, we considered a large vitreoretinal database study in the UK,⁴ which reported that 40.2% of PPVs with macular manipulation were for MH. For the 34,314 German PPV patients with macular manipulation, the pool of MH patients would be 13,795, which is also in good accordance with the OPS/ICD filtered data figure of 15,878 patients. The same UK database study found that 14.2% of PPVs with macular manipulation were for VMT, suggesting that for Germany, 2,255 of the 15,878 vitrectomy patients with macular manipulation had VMT. These results are also concordant.

Weaknesses of this study include a reliance on certain assumptions. First, the AAO classification system describes stage 3 MHs (which we excluded) as those $\geq 400 \mu\text{m}$ in diameter with vitreomacular separation, but it is possible that some MHs $>400 \mu\text{m}$ still had persisting VMA. Also, clinicians may have applied the classification systems variably, as more than one has evolved over time.^{1,3,16} Further, the measurement of MHs and their classification may be subject to significant interobserver variability. The clinical statistic reflects in-patient settings with vitrectomy only, while intravitreal gas or air injections are documented by several case series as the possible out-patient therapy for sVMA.^{17–20}

Conclusion

While our estimated incidence of VMT (with and without MH) in Germany relies on a number of untested assumptions, it, nonetheless, shows that sVMA is an important disease affecting a large number of individuals, many of whom may be undiagnosed or exist outside of the clinic system.

Disclosure

AN: consultant for Alimera, Santen, OD-OS, Contracare, Santhera, Thrombogenics/Oxurion. TJ: former consultant to Thrombogenics and Advisor to Alcon; the employer receives site payments for participants enrolled into clinical trials sponsored by Alcon. The authors report no other conflicts of interest in this work.

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Supplementary materials

Table S1 International epidemiology search

Databases: EMBASE 1974–2018; Medline(R) 1946–2018		
Search engine: Ovid		
Date of search: February 19, 2018		
Period searched: 1946–2018		
Other filters: No filters		
#	Syntax	Hits
#1	vitreomacular traction*.af	1,351
#2	Vitreo macular traction*.af	60
#3	VMT.af	945
#4	VMTS.af	43
#5	vitreomacular adhesion*.af	515
#6	vitreo macular adhesion*.af	8
#7	vitreous and macula* and separation.af	385
#8	VMA.af	2,970
#9	(vitreo-macular traction* or vitreoretinal traction* or vitreo-retinal traction*).af	623
#10	(vitreo-macular adhesion* or vitreoretinal adhesion* or vitreo-retinal adhesion).af	299
#11	macular hole*.af	8,139
#12	(retinal Hole* or retinal break*).af	3,126
#13	Vitreous detachment*.af	3,080
#14	Retinal detachment.af	44,383
#15	macular detachment*.af	1,317
#16	(Macula hole* or FTMH).af	4,774
#17	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	57,973
#18	(epidemiology or incidence or prevalence).af	5,210,928
#19	17 and 18	3,778
#20	limit 19 to yr="1996–2018"	3,039

Table S2 German epidemiology search

Databases: EMBASE 1974–2018 week 9, Medline 1947 to week 4, 2018, Medline Epub ahead of print, in-process, and other non-indexed citation 2014 to present		
Search engine: Ovid		
Date of search: February 19, 2018		
Period searched: 1947–2018		
Other filters: No filters		
#	Syntax	Hits
#1	((vitreomacula* or vitreoretinal or vitreo-macula* or vitreo macula* or vitreo retinal) and traction).af	2,553
#2	(VMT or VMTS).af	983
#3	(vitreomacula* adhesion* or vitreo macula* adhesion*).af	541
#4	(macula* Hole* or macula* foramen or FTMH).af	9,071
#5	#1 OR #2 OR #3 OR #	11,446
#6	(vitrectomy or ppV or pars plana or surgery or operation).af	7,536,471
#7	#5 AND #6	7,882
#8	((((prospective or retrospective or cohort or observational or prognostic) and trial) or analysis or study or factor).af	28,747,371
#9	#14 AND #13	4,499
#10	German\$.af	6,094,077
#11	10 AND 9	719

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