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Vestibular syndromes, diagnosis and diagnostic errors in dizzy patients presenting to the emergency department.

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5 2 Vestibular syndromes, diagnosis and diagnostic errors in dizzy patients presenting to the emergency
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3 28 **ABSTRACT**
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5 29 **Objectives:** Our aim was to determine the frequency of vestibular syndromes, diagnoses, diagnostic
6
7 30 errors and resources used in patients with dizziness in the emergency department (ED).
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10 31 **Design:** Retrospective cross-sectional study
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12 32 **Setting:** Tertiary referral hospital
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15 33 **Participants:** Adult patients presenting with dizziness
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18 34 **Primary and secondary outcome measures:** We collected clinical data from the initial ED report
19
20 35 from 07/2015 until 08/2020 and compared with the follow-up report if available. We calculated the
21
22 36 prevalence of vestibular syndromes and stroke prevalence in dizzy patients. We reported the rate of
23
24 37 diagnostic errors using the follow-up diagnosis as reference standard.
25

26 38 **Results:** We included 1535 patients with dizziness. 19.7% (303) of the patients presented with acute
27
28 39 vestibular syndrome (AVS), 34.7% (533) with episodic vestibular syndrome (EVS), 4.6% (71) with
29
30 40 chronic vestibular syndrome (CVS), and 40.9% (628) with no or unclassifiable vestibular syndrome.
31
32 41 The three most frequent diagnosis were stroke / minor stroke (10.1%, 155), benign paroxysmal
33
34 42 positional vertigo (9.8%, 150) and vestibular neuritis (9.6%, 148). In patients with an AVS 25.4% (77)
35
36 43 had a stroke. The cause of the dizziness remained unknown in 45.0% (692) and 18.0% received a
37
38 44 false diagnosis. In 662 (43.1%) cases follow-up was available and 58.2% with an initially unknown
39
40 45 diagnoses received a final diagnosis. Overall, 69.9% of all 1535 dizzy patients received neuroimaging
41
42 46 (MRI 58.2%, CT 11.6%) in the ED.
43

44 47 **Conclusions:** One fourth of dizzy patients in the ED presented with AVS with a high prevalence (10%)
45
46 48 of vestibular strokes. EVS was more frequent, however, the rate of undiagnosed dizzy patients and the
47
48 49 number of patients receiving neuroimaging was high. Almost half of them still remained without
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50 50 diagnosis and among those diagnosed were often misclassified. Many unclear cases of vertigo could
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52 51 be diagnostically clarified after a follow-up visit.
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57 **Strengths and limitations**

- 58 • This cross-sectional study includes a large number of dizzy patients visiting the emergency
59 department.
- 60 • We report the frequency of vestibular syndromes based on the international classification of
61 the Bárány society.
- 62 • For a more accurate classification into vestibular syndromes a prospective longitudinal study
63 design would be needed
- 64 • We observed a referral bias (tertiary referral center) leading to a higher proportion of
65 dangerous diagnoses in dizzy patients
- 66 • Since the treating clinician decided whether a follow-up was pursued there might be a
67 selection bias

68 **Key words:** vestibular syndromes, acute vestibular syndrome, episodic vestibular syndrome,
69 frequencies, vertigo, dizziness, emergency department, diagnostic errors

71 **BACKGROUND**

72 Patients with dizziness presenting in the emergency department (ED) often suffer from accompanying
73 symptoms such as nausea, vomiting, gait disturbance and motion intolerance, summarized as a
74 vestibular syndrome.[1] There is no direct link to a specific cause such as a peripheral or central
75 disorder,[2] however, physicians might narrow down their differential diagnosis by classifying into three
76 basic categories of vestibular syndromes.[3]: Episodic, acute and chronic vestibular syndrome. Such
77 classification is based on the time course and duration of symptoms as well as on whether the
78 symptoms are continuous or repetitive. This means a paradigm shift from classical teaching,[4] which
79 is focusing on history taking and investigating symptom quality such as vertigo, disequilibrium,
80 presyncope and non-specific dizziness. Previous investigations proved that description of symptom
81 quality is imprecise and inaccurate for diagnostic decisions.[5] The classification into different
82 vestibular syndromes is internationally accepted and was introduced in the recently revised
83 International Classification of Diseases from the World Health Organization (WHO) (ICD-11 and ICD-
84 12 code, 2016).[6] This new definition was elaborated by the international and interdisciplinary Bárány
85 Society. It allows physicians to recognize patterns, to apply different diagnostic tests based on their

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3 86 classification and to reduce the number of differential diagnoses; however, the frequency of vestibular
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5 87 syndromes and their underlying diagnosis remains poorly investigated. In addition, there is an
6
7 88 expected overlap of timing and symptoms within each syndrome since any acute vestibular syndrome
8
9 89 might persist and develop into a chronic disease or might occur repetitively with symptom free
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11 90 intervals.

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13 91 We therefore sought to investigate the frequency of vestibular syndromes, to assess the underlying
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15 92 diagnosis stratified by syndromes, the frequency of diagnostic errors comparing the initial with the
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17 93 follow-up visit and to describe the resource consumption in the ED.

18 19 20 94 **METHODS**

21
22 95 In this retrospective cross-sectional study, we used data collected prospectively during screening for
23
24 96 the DETECT (Dizziness Evaluation Tool for Emergent Clinical Triage) study.[7–10] We were looking
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26 97 for patients presenting to the ED of the Inselspital Bern (University Hospital and tertiary referral
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28 98 hospital) with an AVS and a suspected stroke diagnosis. Research fellows trained in neurotology
29
30 99 prospectively screened and identified dizzy patients from 07/2015 to 08/2020 using either the ED
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32 100 triage software system (chief complaint or a suspected diagnosis) or direct information from the
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34 101 emergency physician. We included all ED patients presenting with dizziness older than 16 years (ED
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36 102 index visit). We use dizziness as an umbrella term throughout the manuscript including the following
37
38 103 set of symptoms: vertigo, dizziness, gait or balance unsteadiness, ataxia and syncope or presyncope.
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40 104 We collected data about baseline demographics, medical history, clinical findings, resources used, as
41
42 105 well as diagnoses. In a second step, we retrospectively compared data from the index visit in the ED
43
44 106 with data collected in patients who received a follow-up examination at our hospital's dizziness clinic
45
46 107 within 90 days after presentation to the ED (follow-up visit).

47 48 108 **Classification of vestibular syndromes**

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50 109 We classified all included patients into 5 categories based on the international classification from the
51
52 110 Bárány Society[1] and predefined criteria:[3] 1) Acute, 2) episodic and 3) chronic vestibular syndrome,
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54 111 4) acute imbalance syndrome and 5) patients not classifiable ("unclear"). We defined vestibular
55
56 112 syndromes as follows:

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59 113 1) *Acute vestibular Syndrome*

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3 114 The acute vestibular syndrome (AVS) is defined as a clinical syndrome of acute onset, continuous
4
5 115 dizziness lasting day to weeks, and generally including features suggestive of new, ongoing vestibular
6
7 116 system dysfunction (e.g., vomiting, nystagmus, severe postural instability).[1] Although this syndrome
8
9 117 is characterized by a single, monophasic event due to a one-time disorder, it might be the beginning of
10
11 118 a recurrent disease or a progressive illness course. Thus, AVS might overlap with other syndromes
12
13 119 explained below or change over time. There are sub classifications of AVS mentioned in the
14
15 120 literature[11] such as t-AVS (post-exposure dizziness after trauma or toxic exposure) or s-AVS
16
17 121 (spontaneous AVS) including all patients with continuous dizziness at rest. For the sake of simplicity,
18
19 122 we classified all these patients under the umbrella term of AVS.

21 123 2) *Episodic vestibular syndrome*

22
23 124 The episodic vestibular syndrome (EVS) is characterized as transient dizziness lasting seconds to
24
25 125 hours, rarely days. It is accompanied by a short duration of nausea, nystagmus and sudden falls.[1]
26
27 126 EVS can occur repetitively (episodes) caused by an episodic disorder with repeated spells, or as a
28
29 127 single event (first manifestation) of a progressive chronic disorder with a transient or recurrent
30
31 128 dizziness. There are subtypes of EVS with associated triggers (t-EVS) or without triggers (s-EVS,
32
33 129 spontaneous EVS). Diagnoses of s-EVS is mainly based on the patient's history. Patients with t-EVS
34
35 130 have often clinical signs such as positional nystagmus after provocation. Both subgroups were
36
37 131 included as EVS without separate differentiation.

38 132 3) *Chronic vestibular syndrome*

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40 133 The chronic vestibular syndrome (CVS) lasts usually months to years and is generally associated with
41
42 134 a persistent vestibular system dysfunction (e.g., oscillopsia, nystagmus, gait unsteadiness, falls).

44 135 4) *Acute imbalance/dysbalance syndrome*

45
46 136 Patients with symptoms that did not meet definitions 1-3 and therefore a vestibular syndrome could be
47
48 137 excluded, were classified as an acute imbalance syndrome (AIS).[12,13] Patients with dizziness as an
49
50 138 isolated symptom and no accompanying symptoms or no nystagmus were therefore classified as
51
52 139 "AIS".

53 140 5) *Unclear vestibular syndrome*

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55 141 If the information in the medical report was not specific enough to decide whether it was a vestibular
56
57 142 syndrome or not, they were labeled as "unclear".

58
59 143 The type of syndromes and diagnoses from the index visit (ED diagnosis) and the follow-up exam
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144 (follow-up or final diagnosis) were analyzed and compared, if available. We only included the main

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3 145 diagnosis reasonable for causing dizziness, additional diagnoses were classified as “other diagnoses”.
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5 146 Patients with more than one differential diagnosis causing dizziness were classified as “unknown”.
6
7 147 Patients were reclassified regarding the type of vestibular syndrome based on the time course of
8
9 148 symptoms and signs. Patients e.g., with symptoms lasting less than 24 hours or with repetitive events
10
11 149 were reported or re-classified as EVS. Misclassified EVS patients were often sent home within a few
12
13 150 hours after symptom onset. Initially misclassified EVS with persistent symptoms, however, were re-
14
15 151 classified as AVS.
16
17 152 We calculated the overall rate of diagnostic errors between the initial ED diagnosis and the follow-up
18
19 153 diagnosis using the follow-up diagnosis as reference standard. We also reported the change of
20
21 154 diagnoses rate stratified by ED diagnoses. The rate of changes of diagnoses at follow-up was
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23 155 calculated as follows: $100 * (1 - \text{correct diagnoses} / \text{total diagnoses ED})$. The diagnosis was assumed
24
25 156 to be correct if it did not change from the initial to the follow-up diagnosis.

27 157 **Statistics**

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29
30 158 We used SPSS (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk,
31
32 159 NY: IBM Corp) for statistics and descriptive data analysis. We did a subgroup analysis on those
33
34 160 patients who received a follow-up examination. Cross tabulations were used to compare results at the
35
36 161 ED index visit with the follow-up visit. Cohen’s Kappa was calculated to report the concordance
37
38 162 between index visit and follow-up regarding the classification of vestibular syndromes and diagnoses.

40 163 **Patient and public involvement**

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42
43 164 Patients or the public were not involved in our research design, conduct, reporting or dissemination
44
45 165 plans.

47 166 **RESULTS**

50 167 **Prevalence of vestibular syndromes and underlying diagnoses**

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52 168 We included 1535 Patients aged from 16 to 98 (mean 55.7 years +/-SD 18.6 years) who presented
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54 169 with dizziness as a chief complaint. Our cohort consisted of 745 (48.5%) men and 790 (51.5%)
55
56 170 women. The age and gender distribution are shown as a histogram in the additional file 1 (figure S1).
57
58 171 Of all patients, 303 presented with AVS (19.7%), 533 with EVS (34.7%), 71 with CVS (4.6%) and 472
59
60 172 patients had an AIS (30.8%). In 156 cases (10.2%), the type of vestibular syndrome remained unclear

173 or was not classifiable based on clinical and reported findings. Since several diagnoses could be
 174 selected, there were more diagnoses than cases.

175 The five most frequent diagnoses including all types of vestibular syndromes were strokes (n=155,
 176 10.1%), benign paroxysmal positional vertigo (BPPV) (n=150, 9.8%), acute unilateral vestibulopathy
 177 (n=148, 9.6%), transient ischemic attack (TIA) (n=77, 5.0%) and dysautonomia (n=63, 4.1%). In 692
 178 cases (45.0%) the diagnosis remained unknown. Table 1 shows the frequency of diagnoses stratified
 179 by vestibular syndromes.

180 **Table 1:** ED diagnoses stratified by vestibular syndromes

Diagnose	total (n=1535)	AVS (n=303)	EVS (n=533)	CVS (n=71)	AIS (n=472)	Unclear (n=156)
Stroke / Minor Stroke	155 (10.10%)	77 (25.41%)	10 (1.88%)	2 (2.82%)	61 (12.92%)	5
BPPV	150 (9.77%)	1 (0.33%)	143 (26.83%)	0 (0.00%)	1 (0.21%)	5
Acute unilateral vestibulopathy (e.g. Vestibular Neuritis)	148 (9.64%)	127 (41.91%)	9 (1.69%)	2 (2.82%)	8 (1.69%)	2
TIA	77 (5.02%)	8 (2.64%)	55 (10.32%)	2 (2.82%)	9 (1.91%)	3
Dysautonomia	63 (4.10%)	0 (0.00%)	14 (2.63%)	1 (1.41%)	47 (9.96%)	1
Vestibular migraine	35 (2.28%)	1 (0.33%)	31 (5.82%)	1 (1.41%)	1 (0.21%)	1
Menière's disease	22 (1.43%)	1 (0.33%)	20 (3.75%)	0 (0.00%)	0 (0.00%)	1
PPPD	22 (1.43%)	1 (0.33%)	2 (0.38%)	9 (12.68%)	7 (1.48%)	3
Tumor	17 (1.11%)	3 (0.99%)	1 (0.19%)	2 (2.82%)	10 (2.12%)	1
Trauma	13 (0.85%)	0 (0.00%)	1 (0.19%)	0 (0.00%)	9 (1.91%)	3
Medical side effects	11 (0.72%)	0 (0.00%)	2 (0.38%)	0 (0.00%)	8 (1.69%)	1
Heart disease	10 (0.65%)	1 (0.33%)	0 (0.00%)	0 (0.00%)	8 (1.69%)	1
Labyrinthitis	9 (0.59%)	7 (2.31%)	1 (0.19%)	1 (1.41%)	0 (0.00%)	0
Infectious disease	7 (0.46%)	6 (1.98%)	0 (0.00%)	1 (1.41%)	0 (0.00%)	0
Metabolic	7 (0.46%)	1 (0.33%)	0 (0.00%)	0 (0.00%)	5 (1.06%)	1
Neurodegenerative disease	5 (0.33%)	1 (0.33%)	0 (0.00%)	0 (0.00%)	4 (0.85%)	0
Acoustic neuroma	4 (0.26%)	1 (0.33%)	0 (0.00%)	2 (2.82%)	1 (0.21%)	0
Vestibular Paroxysmia	1 (0.07%)	0 (0.00%)	1 (0.19%)	0 (0.00%)	0 (0.00%)	0
Others	110 (7.17%)	13 (4.29%)	10 (1.88%)	8 (11.27%)	67 (14.19%)	12
Unknown	692 (45.08%)	62 (20.46%)	239 (44.84%)	44 (61.97%)	228 (44.31%)	119
Total ¹⁾	1558	311	539	75	474	159

181 ¹⁾Since several diagnoses can be selected per case, there are more diagnoses than cases. For each diagnosis
 182 the corresponding syndrome is listed in the table, so the total number of the syndromes is higher.

183 Abbreviations: AVS (acute vestibular syndrome), EVS (episodic vestibular syndrome), CVS (chronich vestibular
 184 syndrome), AIS (acute imbalance syndrome), BPPV (benign paroxysmal positional vertigo), TIA (transient
 185 ischemic attack), PPPD (persistent postural-perceptual dizziness)

186

187 Accuracy of syndrome classification

188 662 (43.1%) out of 1535 patients received a follow-up. There was an excellent agreement (Cohen's
 189 Kappa = 0,909, $p < 0.001$) between the syndrome classification at index visit and follow-up with a
 190 reported change of the acute vestibular syndrome in 3.2% after the follow-up. Most of the misclassified
 191 AVS patients were reassessed as EVS. EVS patients, however, were misclassified in 3.6%. Among
 192 the patients with an AIS on the ED, the re-classification rate was 8.0%, whereas 1 patient was
 193 subsequently classified as AVS. In the cases that could not be initially classified in the ED, 34.7%
 194 could be classified as a vestibular syndrome or AIS in the follow-up examination (table 2).

195 **Table 2:** Cross tabulation - vestibular syndrome ED vs. follow-up (n=662)

		Follow-up						Change of syndrome [%]
		AVS	EVS	CVS	AIS	unclear	total	
ED	AVS	215	5	0	1	1	222	3.15%
	EVS	5	187	0	2	0	194	3.61%
	CVS	0	0	34	0	0	34	0.00%
	AIS	1	6	3	150	3	163	7.98%
	unclear	4	6	2	5	32	49	34.69%
	total	225	204	39	158	36	662	

196

197 Diagnostic errors in dizzy patients

198 In this section, we compare the diagnosis at ED with the diagnosis at follow-up (n=662). We report an
 199 overall change in diagnosis between initial ED assessment and follow-up of 31.4 %. The proportion of
 200 diagnostic errors (excluding patients with unknown causes) was 18.0%. There was a moderate to low
 201 agreement between the initial diagnosis (ED diagnosis) and the final diagnosis after the follow-up
 202 (Cohen's Kappa = 0.609, $p < 0.001$). Often diagnostic errors occurred in patients with dysautonomia
 203 (33%, 6/9), TIA (30.6%, 15/49), BPPV (28.6%, 8/28), Menière's disease (26.7%, 4/15), stroke / minor
 204 stroke (13.6%, 18/132) and for acute unilateral vestibulopathy (15.7%, 14/89). Of the cases with an
 205 initial diagnosis of TIA, the diagnosis was changed during follow-up to "stroke/minor stroke" in seven
 206 and to "unknown" in four cases (table 3 and additional file 1 table S1). The cause of the dizziness was
 207 at the time of the ED visit unknown in 37.6%. In 104 out of 662 cases the diagnosis remained unclear
 208 even after the follow-up exam, however, 58.2% of all unknown cases in the ED received finally a

209 diagnosis and could be clarified (table 4). A special focus was placed on patients with an undiagnosed
 210 dangerous cause of dizziness (strokes / minor strokes, TIA) leading to potential diagnosis-related
 211 harm. There were two patients initially diagnosed with BBPV, three with acute unilateral vestibulopathy
 212 and one case with a medical side effect where the initial diagnosis was changed to TIA or a stroke /
 213 minor stroke at follow-up. Among patients with no specific diagnoses in the ED (classified as
 214 unknown/unclear), 14 patients had a stroke and 9 a TIA. In summary, in 29 of the 662 followed-up
 215 cases (4.4%) a dangerous diagnosis was found at follow-up (potential diagnosis-related harms) which
 216 was initially not diagnosed in the ED (see additional file 1 table S1, bold cases).

217 **Table 3:** Number of diagnostic errors, change of diagnosis rates, missed dangerous diagnoses and
 218 mimics.

ED Diagnoses	Total ED	# of diagnostic errors	Change of diagnosis*	# of missed strokes or TIA	Frequency of undiagnosed underlying diseases (top 3)**
Stroke / Minor stroke	132	18	13.6%	5 (TIA)	TIA (5) Acute unilateral vestibulopathy (4) Dysautonomia (1)
Acute unilateral vestibulopathy (e.g. Vestibular Neuritis)	89	14	15.7%	3	Stroke / Minor stroke (2) Menière (2) Others (2)
TIA	49	15	30.6%	7 (strokes)	Stroke / Minor stroke (7) BPPV (1) Metabolic (1) Medical side effects (1)
BPPV	28	8	28.6%	2	Acute unilateral vestibulopathy (3) Stroke / Minor stroke (2) Others (2)
Menière's disease	15	4	26.7%	0	Acute unilateral vestibulopathy (3) Labyrinthitis (1)
Tumor	14	1	7.1%	0	0
Vestibular migraine	12	3	25.0%	0	Others (2) PPPD (1)
Dysautonomia	9	3	33.3%	0	Others (2) Heart disease (2) Medical side effects (1)
Labyrinthitis	7	2	28.6%	0	Acute unilateral vestibulopathy (1) Acoustic neurinoma (1)
Infectious disease	6	3	50.0%	0	Acute unilateral vestibulopathy (3)
Heart disease	5	0	0.0%	0	0
PPPD	5	0	0.0%	0	0

Others***	42	4	9.5%	0	Dysautonomia (2) BPPV (1) Tumor (1)
Unknown	249	145	58.2%	23	Acute unilateral vestibulopathy (35) Vestibular migraine (22) Stroke / Minor stroke (14) TIA (9)
Total	662	222	31.4%	40	

219 *Since multiple answers were possible for the diagnoses, the number of diagnostic errors did not
220 necessarily correspond to the proportion of change of diagnosis. The rate of changes of diagnoses at
221 follow-up is calculated as follows: $100 * (1 - \text{correct diagnoses} / \text{total diagnoses ED})$.

222 **Undiagnosed underlying diseases: This column shows the most frequent changed diagnosis based
223 on the follow-up exam.

224 ***Diagnoses less frequent than five are not listed in the table.

225 **Table 4:** Unknown ED diagnoses resolved after follow-up

Diagnoses at Follow-up	unknown ED diagnoses (n=249)	Frequency
Acute unilateral vestibulopathy (e.g. Vestibular Neuritis)	35	14.06%
Others	28	11.24%
Vestibular migraine	22	8.84%
Stroke	14	5.62%
TIA	9	3.61%
Dysautonomia	8	3.21%
Menière's disease	8	3.21%
BPPV	6	2.41%
PPPD	6	2.41%
Unknown etiology central vestibular syndrome	4	1.61%
Metabolic disorders	3	1.20%
Tumor	1	0.40%
Medical side effects	1	0.40%
Heart disease	1	0.40%
Labyrinthitis	1	0.40%
Infectious disease	1	0.40%
Trauma	0	0.00%
Neurodegenerative disease	0	0.00%
Acoustic neuroma	0	0.00%
Unknown	104	41.77%

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228

229 ED resource use

230 Overall, 69.9% of all 1535 dizzy patients received neuroimaging at the ED visit (MRI 58.2%, CT
 231 11.6%). 16.8% of stroke patients underwent a computed tomography (CT), 89.7% an MRI. Patients
 232 with a BPPV received in 41.3% an MRI and in 8% a CT showing a similar resource use as patients
 233 with acute unilateral vestibulopathy (48% MRI, 6.8% CT). Table 5 shows details of ED resource use
 234 stratified by ED diagnoses.

235 **Table 5:** ED Resources stratified by diseases (n=1535)

	Stroke / Minor Stroke	BPPV	Acute unilateral vestibulopathy	TIA	Menière's disease	PPPD	Trauma
MRI	139 (89.7%)	62 (41.3%)	71 (48.0%)	62 (80.5%)	11 (50.0%)	9 (40.9%)	3 (23.1%)
CT	26 (16.8%)	12 (8.0%)	10 (6.8%)	13 (16.9%)	0 (0.0%)	0 (0.0%)	6 (46.2%)
Audiology	5 (3.2%)	16 (10.7%)	90 (60.8%)	6 (7.8%)	12 (54.5%)	1 (4.5%)	0 (0.0%)
Caloric	8 (5.2%)	26 (17.3%)	115 (77.7%)	11 (14.3%)	9 (40.9%)	2 (9.1%)	0 (0.0%)
vHIT	4 (2.6%)	6 (4.0%)	41 (27.7%)	3 (3.9%)	2 (9.1%)	1 (4.5%)	0 (0.0%)
Total diagnoses	155	150	148	77	22	22	13

237 DISCUSSION

238 One fifth to one third of dizzy patients presented symptoms consisting of AVS or EVS. Another third of
 239 patients were not classifiable based on current criteria. Patients with CVS were noticeably less likely to
 240 present to the ED. In more than one third of the cases, which received a follow-up, the diagnosis was
 241 changed. Diagnostic uncertainty could be resolved at the follow-up visit in more than half of patients
 242 with unknown or unclear diagnosis. We found that a great number of imaging studies were ordered for
 243 dizziness workup.

244 Prevalence of vestibular syndromes and underlying diagnoses

245 The reported prevalence of AVS in the literature ranges from 10% to 22%, [2, 14] which matches our
 246 findings in the ED (20%). Our reported prevalence in the ED is not generalizable to other settings such
 247 as outpatient clinics, where the proportion of chronic vestibular syndromes might predominate. Violent
 248 vertigo attacks in patients with recurrent vertigo (EVS) might prompt patients to visit the ED rather than
 249 an outpatient clinic resulting in a high prevalence of 35%. The most common ED diagnoses in the total

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3 250 ED population were stroke / minor stroke, BPPV, and acute unilateral vestibulopathy, which is in
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5 251 agreement with other reports.[15,16] The ED prevalence of strokes / minor stroke was 10% in our
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7 252 study, which is considerably higher than previously described (~4% cerebrovascular).[15,17] The
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9 253 reported prevalence, however is consistent with our previous, retrospective study from the same
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11 254 center with another sample.[18] In patients with AVS, however, the prevalence of stroke is significantly
12
13 255 higher at 25.4% probably due to a referral bias of a tertiary care center including the largest stroke
14
15 256 center of the country. Despite extensive investigations reflected in the resources used, almost half of
16
17 257 the cases remained undiagnosed, which is higher compared to 22% in another cross-sectional
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19 258 study.[15] One reason for the higher number of “unknown” causes could be due to the applied
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21 259 classification rules classifying patients with multiple differential diagnoses as “unknown”.

22 23 260 **Accuracy of syndrome classification**

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25 261 Overall, the accuracy of the classification into three different vestibular syndromes was high. In one-
26
27 262 tenth of the cases, the documented history was not sufficient to decide whether the patient had a
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29 263 vestibular syndrome. Possible reasons for this were a lack of documentation or an inappropriate
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31 264 history taking. In the group with a follow-up examination, more than one third of the unclear ED cases
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33 265 could be assigned to a vestibular syndrome or a vestibular syndrome could be excluded based on the
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35 266 extended history of the follow-up report. This finding emphasizes the importance of taking a targeted
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37 267 history (asking timing and triggers)[11,19] and the need of a follow-up to better assess the time course
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39 268 of dizziness. Digital decision support tools might assist physicians to take a structured and complete
40
41 269 history. It is therefore important to improve digital competencies in the future.[20] Overall, there were
42
43 270 only a few misclassifications of vestibular syndromes in the ED. Misclassified EVS patients presenting
44
45 271 initially as AVS had a short duration of symptoms which abated after the ED discharge. Diagnoses
46
47 272 with EVS being at risk for misclassification as AVS included vestibular migraine, Menière’s disease
48
49 273 and TIA. Main reason for misclassification was the first time occurrence of episodic dizziness with no
50
51 274 previous history of dizzy episodes as mandated by international diagnostic criteria.[21,22] We also
52
53 275 found misclassifications of AVS as EVS in patients with cerebral strokes, vestibular neuritis and with
54
55 276 dysautonomia. Infarctions in the cerebellum (mainly PICA territory) can mimic positional vertigo,
56
57 277 known as pseudo-BPPV.[23] Finally, each patient with an AVS suffers from motion intolerance, which
58
59 278 can be misinterpreted as positional vertigo.

60 279

280 **Diagnostic errors in dizziness patients**

281 The terminology and definitions regarding diagnostic errors is under debate.[24] It can be used as an
282 umbrella term including preventable, reducible or unavoidable diagnostic errors.[25] Our data,
283 however, were not sufficient to assess the underlying diagnostic processes and workups leading to a
284 specific diagnosis. We avoided, therefore, terms such as 'misdiagnosis', because such conclusions
285 might be perceived as implicating errors in the diagnostic process, which we did not investigate. A sub
286 classification into diagnostic process failure or diagnostic label failure was not possible based on our
287 design. Diagnosing dizziness is a challenge for ED physicians and diagnostic errors are unavoidable
288 even for experts in the field (following an optimal diagnostic process) due to the nature and complexity
289 of the underlying diseases.[26] Thus, we aim to increase awareness about an unresolved issue
290 regarding diagnostic accuracy in dizzy patients visiting the ED. In a German retrospective study, 124
291 of 475 dizziness patients (26%) received follow-up.[16] This number is lower than the number of
292 patients followed up in our study (43.1%). This selection bias has to be kept in mind, interpreting the
293 presented results. The decision to schedule patients for follow-up could reflect an intimate uncertainty
294 with the diagnosis or be an expression of increased caution of the treating physician with that
295 particular patient. In another study from our department on diagnostic errors the "feeling of atypical
296 presentation" was the only predictor of a diagnostic error.[27] This "feeling of atypical presentation" is
297 likely to prompt follow-up visits leading to a selection bias in our follow-up patients. In the German
298 study, ED diagnosis was corrected in 43%.[16] We observed a lower rate of diagnostic errors in our
299 study (31%). Of the benign ED diagnoses, 6% (n= 7 of 124) were finally diagnosed with a dangerous
300 diagnosis during follow-up in the German study[16] compared to 4% (n= 29 of 662) in our study.
301 Patients in our study, however, received significantly more often MRIs in the ED (58% MRI vs. 18%).
302 This might contribute to the lower number of missed dangerous diagnoses (diagnosis related harm).
303 Despite extensive ED workups (including neuroimaging), four patients were still diagnosed as
304 vestibular neuritis or BPPV and finally had a stroke (Pseudo-neuritis or Pseudo-BPPV) without any
305 focal neurological signs. Recent literature confirms that 50% of patients with vestibular strokes might
306 have isolated dizziness.[28,29] The MRI misses 10-20% of strokes presenting with AVS during the first
307 24-48h after onset.[30] Up to 50% false negative MRIs are reported for smaller vestibular strokes
308 (<1cm).[28] The 'HINTS' examination can be a possible solution for this dilemma. This three-step
309 bedside exam, introduced in 2009,[31] includes the head impulse test, nystagmus test and test of
310 skew and is more sensitive for stroke than early MRI. The application of a portable device using an

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3 311 eye-tracker and head accelerometers allows a quantitative and accurate stroke prediction in patients
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5 312 with AVS.[7,32–34] The comparison between diagnoses at the index (ED) and the follow-up visit
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7 313 shows that in many cases a definite diagnosis can only be made over time. This is often due to
8
9 314 diagnostic criteria that require repetitive episodes of vertigo.[21,22] Some patients are symptom-free in
10
11 315 the interval between episodes of dizziness or at the time of the emergency visit.

13 316 **ED resource use**

16 317 Altogether, neuroimaging was ordered in 70% of cases, of which 83% were MRIs. This high
17
18 318 percentage may be due to the 7/24-availability of MR imaging in our university hospital. We observed
19
20 319 that a large number of MRI was performed in patients who finally received a peripheral vestibular
21
22 320 diagnosis such as BPPV, Menière's disease or an acute unilateral vestibulopathy. The diagnosis of
23
24 321 vestibular disorders can often be established by targeted history taking and clinical examination. There
25
26 322 is no need for neuroimaging in clinical diagnoses such as BPPV with a typical history and typical
27
28 323 positional nystagmus elicited by diagnostic maneuvers.[35] Atypical findings (e.g. in BPPV with
29
30 324 apogeotropic nystagmus) or a diagnosis of exclusion (e.g. in Menière's disease) might still justify
31
32 325 neuroimaging (MRI) in the ED. CT scans, however, are only suggested in patients with suspected
33
34 326 trauma, hemorrhage or in patients with a contraindication for a MRI. The current clinical approach
35
36 327 leads to an unnecessary overuse of computed tomography and magnetic resonance imaging and
37
38 328 increases costs exceeding billions of dollars in the US alone.[36] Dizzy patients have longer average
39
40 329 ED stays than patients without dizziness because they undergo more testing.[15] The rate of
41
42 330 undiagnosed or misclassified patients remains high, resulting in higher costs and considerable waste
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44 331 of resources in the ED in Switzerland.[36–38]

45 332 **Strengths and limitations**

48 333 The strengths of the study are the large number of included and screened cases and the
49
50 334 determination of vestibular syndromes based on history and follow-up assessments. A more accurate
51
52 335 classification into the vestibular syndromes would need, however, a prospective longitudinal study
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54 336 design. We also observed a referral bias (tertiary referral center) leading to a higher proportion of
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56 337 dangerous diagnoses in dizzy patients. In addition, the treating clinician decided whether a follow-up
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58 338 was pursued, which may have caused a selection bias.

59 339 **Implications for clinicians**

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3 340 Our study confirms that about a fifth of patients suffers from AVS. The high prevalence of strokes in
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5 341 patients with continuous dizziness (25%), the high number of undiagnosed or misclassified cases
6
7 342 should increase the overall awareness regarding diagnostic errors and stroke mimics. Consequently,
8
9 343 we suggest a three-stage diagnostic test process for patients presenting with dizziness in the ED. This
10
11 344 approach does intend increase diagnostic accuracy and to reduce neuroimaging in the acute stage.
12
13 345 We suggest, therefore,

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15 346 1) A more sensitive screening (triage) test including a classification into vestibular syndromes
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17 347 (targeted history) and recording of spontaneous nystagmus, 2) a targeted clinical exam with either
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19 348 "HINTS" test[31] in AVS patients or "Dix-Hallpike" examination[35] in EVS patients with triggers and 3)
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21 349 a dedicated neuroimaging (e.g. acute and delayed MRI) in patients with suspected central causes of
22
23 350 vertigo.

24
25 351 In patients with EVS and absence of triggers (suspected Menière's disease or vestibular migraine) we
26
27 352 alternatively suggest as a second stage caloric testing and audiometry in a planned follow-up and as a
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29 353 third stage a delayed neuroimaging (diagnosis of exclusion). Patients without any nystagmus
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31 354 (spontaneous or after provocation) might need a more extended neurological exam such as BE-
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33 355 FAST.[39] Patients with inconclusive or atypical findings might need further assessment for risk factors
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35 356 (e.g. ABCD2 score)[40] in order to minimize the risk for missed minor strokes and to prevent future
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37 357 harmful events. We further recommend a low threshold for organizing a follow-up appointment in dizzy
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39 358 patients since the symptoms and the diagnosis might change over time. This study paves the way for
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41 359 future studies providing epidemiological data including the expected prevalence for each type of
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43 360 vestibular syndrome.

44 45 361 **CONCLUSION**

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48 362 One fifth of dizzy patients in the ED presented with AVS with a high prevalence (10%) of vestibular
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50 363 strokes. Episodic vertigo (EVS) was more frequent, however, the rate of undiagnosed dizzy patients
51
52 364 and the number of patients receiving neuroimaging was high. Almost half of them still remained
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54 365 without diagnosis and among those diagnosed were often misclassified. Many unclear cases of vertigo
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56 366 could be diagnostically clarified after a follow-up visit.

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3 370 **ABBREVIATIONS**
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6 371 ED emergency department
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8 372 AVS acute vestibular syndrome
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10 373 EVS episodic vestibular syndrome
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12 374 AIS acute imbalance syndrome
13
14 375 CVS chronic vestibular syndrome
15
16 376 TIA transient ischemic attack
17
18 377 BPPV benign paroxysmal positional vertigo
19
20 378 AUVP acute unilateral vestibulopathy
21
22 379 MRI magnetic resonance imaging
23
24 380 CT computer tomography
25
26 381 vHIT video head impulse test
27
28 382 PPPD persistent postural-perceptual dizziness
29
30 383 VOG video-oculography
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33 385 **DECLARATIONS**

34 386 **Ethics approval and consent to participate:** The study was approved by the local ethics committee
35
36 387 (KEK Bern, #2021-00918). Given the retrospective nature of the study, informed consent was provided
37
38 388 through a hospital-wide general consent. Patients who withdrew consent for evaluation of their medical
39
40 389 data were excluded in accordance with legal requirements.

41
42 390 **Consent for publication:** Not applicable

43
44 391 **Availability of data and materials:** The datasets used and/or analyzed during the current study are
45
46 392 available from the corresponding author on reasonable request.

47
48 393 **Competing interests:** None of the investigators has any relevant financial interests, activities,
49
50 394 relationships, or affiliations that represent a relevant financial conflict of interest with respect to the
51
52 395 conduct or analysis of this study.

53
54
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56
57 397 **Authors' contributions:** AK, EZ, FN and LC collected and processed the data. GM and LC conceived
58
59 398 the study, analyzed and interpreted the data and wrote the draft. MC, TS, WH and SJ were involved in
60

1
2
3 399 the interpretation of the data and in the review. All authors discussed the results, commented on the
4
5 400 manuscript, and read and approved the final version.
6

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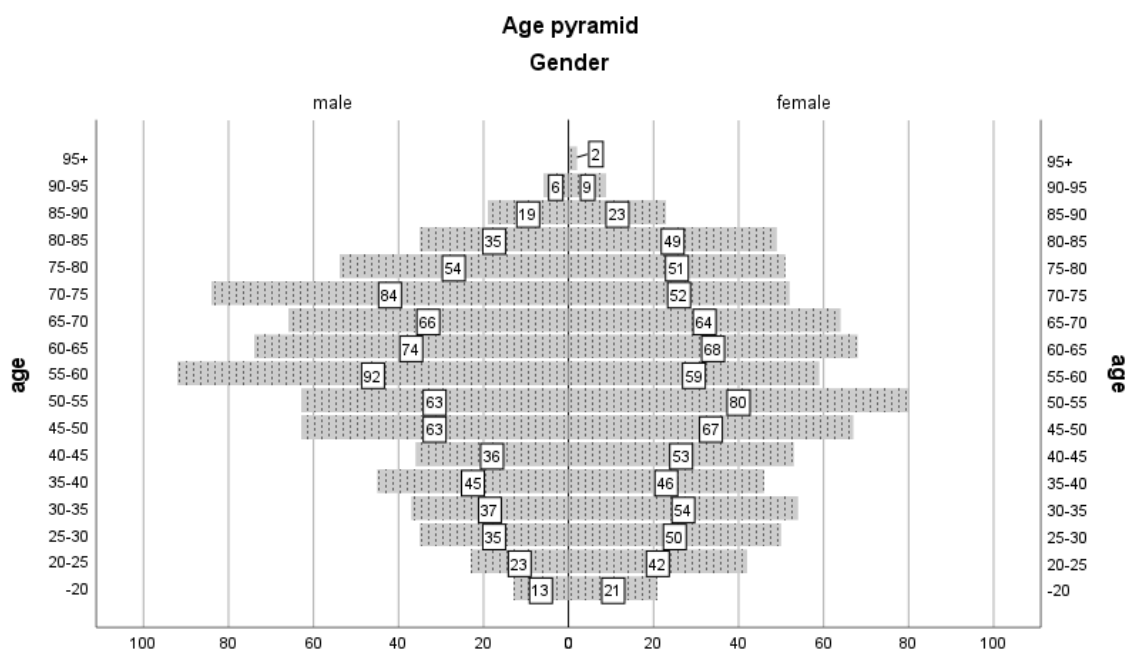
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Vestibular syndromes, diagnosis and diagnostic errors in dizzy patients presenting to the emergency department. (Comolli et al.)

APPENDIX

Figure S1



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Frequencies of vestibular syndromes, diagnosis and misdiagnosis rates in a tertiary emergency department (Comolli et al.)

Table S1: Cross table diagnoses emergency department (ED) vs. Follow-up

Bold cases represent the 29/662 (4.4%) cases where a dangerous diagnosis was found during follow-up but not during ED workup

	Diagnoses follow up																				Change of diagnoses at follow-up ²⁾	
	Stroke / Minor Stroke	BPPV	Vestibular Deficit (e.g. Vestibular Neuritis)	TIA	Dysautonomia	Vestibular migraine	Menière's disease	PPPD	Tumor	Trauma	Medical side effects	Heart disease	Labyrinthitis	Infectious disease	Metabolic disorders	Neurodegenerative disease	Acoustic neuroma	Others	unknown	unknown etiology central vestibular syndrome		Total Diagnoses ED ¹⁾
Stroke / Minor Stroke	114	0	4	5	1	0	0	0	0	0	0	0	0	0	0	0	0	1	4	3	132	13.6%
BPPV	2	20	3	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2	2	0	28	28.6%
Vestibular Deficit (e.g. Vestibular Neuritis)	2	0	75	1	0	1	2	0	0	0	0	0	1	0	0	1	1	2	6	0	89	15.7%
TIA	7	1	0	34	0	0	0	0	0	0	1	0	0	0	1	0	0	0	4	1	49	30.6%
Dysautonomia	0	0	0	0	6	0	0	0	0	0	1	2	0	0	0	0	0	2	0	0	9	33.3%
Vestibular migraine	0	0	0	0	0	9	0	1	0	0	0	0	0	0	0	0	0	2	1	0	12	25.0%
Menière's disease	0	0	3	0	0	0	11	0	0	0	0	0	1	0	0	0	0	1	0	0	15	26.7%
PPPD	0	0	0	0	0	1	0	5	0	0	0	0	0	0	0	0	0	0	0	0	5	0.0%
Tumor	0	0	0	0	0	0	0	0	13	0	0	0	0	0	0	0	0	0	1	0	14	7.1%
Trauma	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	3	0.0%
Medical side effects	1	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	3	33.3%
Heart disease	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0	5	0.0%
Labyrinthitis	0	0	1	0	0	0	0	0	0	0	0	0	5	3	0	0	1	0	0	0	7	28.6%
Infectious disease	0	0	3	0	0	0	0	0	0	0	0	0	1	3	0	0	0	0	0	0	6	50.0%
Metabolic disorders	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0.0%
Neurodegenerative disease	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	1	0	0	0	3	33.3%
Acoustic neuroma	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	4	0	0	0	4	0.0%
Others	0	1	0	0	2	0	0	0	1	0	0	0	0	0	0	0	0	38	1	0	42	9.5%
unknown	14	6	35	9	8	22	8	6	1	0	1	1	1	1	3	0	0	28	104	4	249	58.2%
Total Diagnoses Follow up ¹⁾	138	28	122	49	17	32	21	11	15	3	4	8	9	5	5	3	5	73	122	8	662	

¹⁾The fields "total" refer to the number of the corresponding diagnosis. Since several diagnoses are possible, the columns and rows do not add up.

²⁾ The rate of changes of diagnoses at follow-up is calculated as follows: $100 * (1 - \text{correct diagnoses (grey fields)} / \text{total diagnoses ED})$

BPPV = benign paroxysmal positional vertigo; TIA= transient ischemic attack; PPPD = persistent postural-perceptual dizziness

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3/4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(b) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6
		(b) Describe any methods used to examine subgroups and interactions	6
		(c) Explain how missing data were addressed	5/6
		(d) If applicable, explain how loss to follow-up was addressed	not applicable
		(e) Describe any sensitivity analyses	not applicable
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6/7
		(b) Give reasons for non-participation at each stage	16
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6-11
		(c) Summarise follow-up time (eg, average and total amount)	7/8
Outcome data	15*	Report numbers of outcome events or summary measures over time	6-11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	not applicable
		(b) Report category boundaries when continuous variables were categorized	not applicable
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-15
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Vestibular syndromes, diagnosis and diagnostic errors in dizzy patients presenting to the emergency department. A cross-sectional study.

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1
2
3 1 **TITLE**
4

5 2 Vestibular syndromes, diagnosis and diagnostic errors in dizzy patients presenting to the emergency
6 3 department. A cross-sectional study.
7
8
9

10 4
11
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28 **ABSTRACT**

29 **Objectives:** Our aim was to determine the frequency of vestibular syndromes, diagnoses, diagnostic
30 errors and resources used in patients with dizziness in the emergency department (ED).

31 **Design:** Retrospective cross-sectional study

32 **Setting:** Tertiary referral hospital

33 **Participants:** Adult patients presenting with dizziness

34 **Primary and secondary outcome measures:** We collected clinical data from the initial ED report
35 from 07/2015 until 08/2020 and compared with the follow-up report if available. We calculated the
36 prevalence of vestibular syndromes and stroke prevalence in dizzy patients. Vestibular syndromes are
37 differentiated in acute (AVS) (e.g., stroke, neuritis vestibularis), episodic (EVS) (e.g., BPPV, TIA) and
38 chronic (CVS) (e.g., PPPD) vestibular syndrome. We reported the rate of diagnostic errors using the
39 follow-up diagnosis as reference standard.

40 **Results:** We included 1535 patients with dizziness. 19.7% (303) of the patients presented with AVS,
41 34.7% (533) with EVS, 4.6% (71) with CVS, and 40.9% (628) with no or unclassifiable vestibular
42 syndrome. The three most frequent diagnosis were stroke / minor stroke (10.1%, 155), benign
43 paroxysmal positional vertigo (9.8%, 150) and vestibular neuritis (9.6%, 148). In patients with an AVS
44 25.4% (77) had a stroke. The cause of the dizziness remained unknown in 45.0% (692) and 18.0%
45 received a false diagnosis. In 662 (43.1%) cases follow-up was available and 58.2% with an initially
46 unknown diagnoses received a final diagnosis. Overall, 69.9% of all 1535 dizzy patients received
47 neuroimaging (MRI 58.2%, CT 11.6%) in the ED.

48 **Conclusions:** One fourth of dizzy patients in the ED presented with AVS with a high prevalence (10%)
49 of vestibular strokes. EVS was more frequent, however, the rate of undiagnosed dizzy patients and the
50 number of patients receiving neuroimaging was high. Almost half of them still remained without
51 diagnosis and among those diagnosed were often misclassified. Many unclear cases of vertigo could
52 be diagnostically clarified after a follow-up visit.

56 **Strengths and limitations**

- 1
2
3 57 • This cross-sectional study includes a large number of dizzy patients visiting the emergency
4
5 58 department.
- 6
7 59 • We report the frequency of vestibular syndromes based on the international classification of
8
9 60 the Bárány society.
- 10
11 61 • For a more accurate classification into vestibular syndromes a prospective longitudinal study
12
13 62 design would be needed
- 14
15 63 • We observed a referral bias (tertiary referral center) leading to a higher proportion of
16
17 64 dangerous diagnoses in dizzy patients
- 18
19 65 • Since the treating clinician decided whether a follow-up was pursued there might be a
20
21 66 selection bias

22
23 67 **Key words:** vestibular syndromes, acute vestibular syndrome, episodic vestibular syndrome,
24
25 68 frequencies, vertigo, dizziness, emergency department, diagnostic errors

26
27
28
29
30 70 **BACKGROUND**

31
32
33 71 Patients with dizziness presenting in the emergency department (ED) often suffer from accompanying
34
35 72 symptoms such as nausea, vomiting, gait disturbance and motion intolerance, summarized as a
36
37 73 vestibular syndrome.[1] There is no direct link to a specific cause such as a peripheral or central
38
39 74 disorder,[2] however, physicians might narrow down their differential diagnosis by classifying into three
40
41 75 basic categories of vestibular syndromes.[3]: Episodic, acute and chronic vestibular syndrome. Such
42
43 76 classification is based on the time course and duration of symptoms as well as on whether the
44
45 77 symptoms are continuous or repetitive. This means a paradigm shift from classical teaching,[4] which
46
47 78 is focusing on history taking and investigating symptom quality such as vertigo, disequilibrium,
48
49 79 presyncope and non-specific dizziness. Previous investigations proved that description of symptom
50
51 80 quality is imprecise and inaccurate for diagnostic decisions.[5] The classification into different
52
53 81 vestibular syndromes is internationally accepted and was introduced in the recently revised
54
55 82 International Classification of Diseases from the World Health Organization (WHO) (ICD-11 and ICD-
56
57 83 12 code, 2016).[6] This new definition was elaborated by the international and interdisciplinary Bárány
58
59 84 Society. It allows physicians to recognize patterns, to apply different diagnostic tests based on their
60
85 classification and to reduce the number of differential diagnoses; however, the frequency of vestibular

1
2
3 86 syndromes and their underlying diagnosis remains poorly investigated. In addition, there is an
4
5 87 expected overlap of timing and symptoms within each syndrome since any acute vestibular syndrome
6
7 88 might persist and develop into a chronic disease or might occur repetitively with symptom free
8
9 89 intervals.

10
11 90 We therefore sought to investigate the frequency of vestibular syndromes, to assess the underlying
12
13 91 diagnosis stratified by syndromes, the frequency of diagnostic errors comparing the initial with the
14
15 92 follow-up visit and to describe the resource consumption in the ED.

17 93 **METHODS**

18
19
20 94 In this retrospective cross-sectional study, we used data collected prospectively during screening for
21
22 95 the DETECT (Dizziness Evaluation Tool for Emergent Clinical Triage) study.[7–10] The sample size
23
24 96 for this study was given through the DETECT study, where a sample size of 200 Patients with an AVS
25
26 97 was needed. We used the screening data which was needed to recruit these 200 patients. We were
27
28 98 looking for patients presenting to the ED of the Inselspital Bern (University Hospital and tertiary referral
29
30 99 hospital) with an AVS and a suspected stroke diagnosis. Research fellows trained in neurotology
31
32 100 prospectively screened and identified dizzy patients during daytime hours from 07/2015 to 08/2020
33
34 101 using either the ED triage software system (chief complaints such as “dizziness”, “vertigo”,
35
36 102 “unsteadiness”, “presyncope”, “vomiting”, “nausea” or a suspected diagnosis) or direct information
37
38 103 from the emergency physician. We included all ED patients presenting with dizziness older than 16
39
40 104 years (ED index visit). We use dizziness as an umbrella term throughout the manuscript including the
41
42 105 following set of symptoms: vertigo, dizziness, gait or balance unsteadiness, ataxia and syncope or
43
44 106 presyncope. We collected data about baseline demographics, medical history, clinical findings,
45
46 107 resources used, as well as diagnoses. In a second step, we retrospectively compared data from the
47
48 108 index visit in the ED with data collected in patients who received a follow-up examination at our
49
50 109 hospital’s dizziness clinic within 90 days after presentation to the ED (follow-up visit).

51 110 **Classification of vestibular syndromes**

52
53
54 111 We classified all included patients into 5 categories based on the international classification from the
55
56 112 Bárány Society[1] and predefined criteria:[3] 1) Acute, 2) episodic and 3) chronic vestibular syndrome,
57
58 113 4) acute imbalance syndrome and 5) patients not classifiable (“unclear”). We defined vestibular
59
60 114 syndromes as follows:

1
2
3 115 1) *Acute vestibular Syndrome*
4

5
6 116 The acute vestibular syndrome (AVS) is defined as a clinical syndrome of acute onset, continuous
7
8 117 dizziness lasting day to weeks, and generally including features suggestive of new, ongoing vestibular
9
10 118 system dysfunction (e.g., vomiting, nystagmus, severe postural instability).[1] Although this syndrome
11
12 119 is characterized by a single, monophasic event due to a one-time disorder, it might be the beginning of
13
14 120 a recurrent disease or a progressive illness course. Thus, AVS might overlap with other syndromes
15
16 121 explained below or change over time. There are sub classifications of AVS mentioned in the
17
18 122 literature[11] such as t-AVS (post-exposure dizziness after trauma or toxic exposure) or s-AVS
19
20 123 (spontaneous AVS) including all patients with continuous dizziness at rest. For the sake of simplicity,
21
22 124 we classified all these patients under the umbrella term of AVS.

23
24 125 2) *Episodic vestibular syndrome*

25
26 126 The episodic vestibular syndrome (EVS) is characterized as transient dizziness lasting seconds to
27
28 127 hours, rarely days. It is accompanied by a short duration of nausea, nystagmus and sudden falls.[1]
29
30 128 EVS can occur repetitively (episodes) caused by an episodic disorder with repeated spells, or as a
31
32 129 single event (first manifestation) of a progressive chronic disorder with a transient or recurrent
33
34 130 dizziness. There are subtypes of EVS with associated triggers (t-EVS) or without triggers (s-EVS,
35
36 131 spontaneous EVS). Diagnoses of s-EVS is mainly based on the patient's history. Patients with t-EVS
37
38 132 have often clinical signs such as positional nystagmus after provocation. Both subgroups were
39
40 133 included as EVS without separate differentiation.

41 134 3) *Chronic vestibular syndrome*

42
43 135 The chronic vestibular syndrome (CVS) lasts usually months to years and is generally associated with
44
45 136 a persistent vestibular system dysfunction (e.g., oscillopsia, nystagmus, gait unsteadiness, falls).

46
47 137 4) *Acute imbalance/dysbalance syndrome*

48
49 138 Patients with symptoms that did not meet definitions 1-3 and therefore a vestibular syndrome could be
50
51 139 excluded, were classified as an acute imbalance syndrome (AIS).[12,13] Patients with dizziness as an
52
53 140 isolated symptom and no accompanying symptoms or no nystagmus were therefore classified as
54
55 141 "AIS".

56 142 5) *Unclear vestibular syndrome*

57
58 143 If the information in the medical report was not specific enough to decide whether it was a vestibular
59
60 144 syndrome or not, they were labeled as "unclear".

1
2
3 145 The type of syndromes and diagnoses from the index visit (ED diagnosis) and the follow-up exam
4
5 146 (follow-up or final diagnosis) were analyzed and compared, if available. We only included the main
6
7 147 diagnosis reasonable for causing dizziness, additional diagnoses were classified as “other diagnoses”.
8
9 148 Patients with more than one differential diagnosis causing dizziness were classified as “unknown”.
10
11 149 Patients were reclassified regarding the type of vestibular syndrome based on the time course of
12
13 150 symptoms and signs. Patients e.g., with symptoms lasting less than 24 hours or with repetitive events
14
15 151 were reported or re-classified as EVS. Misclassified EVS patients were often sent home within a few
16
17 152 hours after symptom onset. Initially misclassified EVS with persistent symptoms, however, were re-
18
19 153 classified as AVS.

20
21 154 We calculated the overall rate of diagnostic errors between the initial ED diagnosis and the follow-up
22
23 155 diagnosis using the follow-up diagnosis as reference standard. We also reported the change of
24
25 156 diagnoses rate stratified by ED diagnoses. The rate of changes of diagnoses at follow-up was
26
27 157 calculated as follows: $100 * (1 - \text{correct diagnoses} / \text{total diagnoses ED})$. The diagnosis was assumed
28
29 158 to be correct if it did not change from the initial to the follow-up diagnosis.

30 31 159 **Statistics**

32
33 160 We used SPSS (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk,
34
35 161 NY: IBM Corp) for statistics and descriptive data analysis. We did a subgroup analysis on those
36
37 162 patients who received a follow-up examination. Cross tabulations were used to compare results at the
38
39 163 ED index visit with the follow-up visit. Cohen’s Kappa was calculated to report the concordance
40
41 164 between index visit and follow-up regarding the classification of vestibular syndromes and diagnoses.
42
43 165 We defined a change in the diagnosis at the follow-up as a diagnostic error.

44 45 46 166 **Patient and public involvement**

47
48 167 Patients or the public were not involved in our research design, conduct, reporting or dissemination
49
50 168 plans.

51 52 53 169 **RESULTS**

54 55 56 170 **Prevalence of vestibular syndromes and underlying diagnoses**

57
58 171 We included 1535 Patients aged from 16 to 98 (mean 55.7 years +/-SD 18.6 years) who presented
59
60 172 with dizziness as a chief complaint. Our cohort consisted of 745 (48.5%) men and 790 (51.5%)

173 women. The age and gender distribution are shown as a histogram in the additional file 1 (figure S1).
 174 Of all patients, 303 presented with AVS (19.7%), 533 with EVS (34.7%), 71 with CVS (4.6%) and 472
 175 patients had an AIS (30.8%). In 156 cases (10.2%), the type of vestibular syndrome remained unclear
 176 or was not classifiable based on clinical and reported findings. Since several diagnoses could be
 177 selected, there were more diagnoses than cases.

178 The five most frequent diagnoses including all types of vestibular syndromes were strokes (n=155,
 179 10.1%), benign paroxysmal positional vertigo (BPPV) (n=150, 9.8%), acute unilateral vestibulopathy
 180 (n=148, 9.6%), transient ischemic attack (TIA) (n=77, 5.0%) and dysautonomia (n=63, 4.1%). In 692
 181 cases (45.0%) the diagnosis remained unknown. A dysautonomia was diagnosed when the “Schellong
 182 test” was positive.[14] Table 1 shows the frequency of diagnoses stratified by vestibular syndromes.

183 **Table 1:** ED diagnoses stratified by vestibular syndromes

Diagnose	total (n=1535)	AVS (n=303)	EVS (n=533)	CVS (n=71)	AIS (n=472)	Unclear (n=156)
Stroke / Minor Stroke	155 (10.10%)	77 (25.41%)	10 (1.88%)	2 (2.82%)	61 (12.92%)	5
BPPV	150 (9.77%)	1 (0.33%)	143 (26.83%)	0 (0.00%)	1 (0.21%)	5
Acute unilateral vestibulopathy (e.g. Vestibular Neuritis)	148 (9.64%)	127 (41.91%)	9 (1.69%)	2 (2.82%)	8 (1.69%)	2
TIA	77 (5.02%)	8 (2.64%)	55 (10.32%)	2 (2.82%)	9 (1.91%)	3
Dysautonomia	63 (4.10%)	0 (0.00%)	14 (2.63%)	1 (1.41%)	47 (9.96%)	1
Vestibular migraine	35 (2.28%)	1 (0.33%)	31 (5.82%)	1 (1.41%)	1 (0.21%)	1
Menière's disease	22 (1.43%)	1 (0.33%)	20 (3.75%)	0 (0.00%)	0 (0.00%)	1
PPPD	22 (1.43%)	1 (0.33%)	2 (0.38%)	9 (12.68%)	7 (1.48%)	3
Tumor	17 (1.11%)	3 (0.99%)	1 (0.19%)	2 (2.82%)	10 (2.12%)	1
Trauma	13 (0.85%)	0 (0.00%)	1 (0.19%)	0 (0.00%)	9 (1.91%)	3
Medical side effects	11 (0.72%)	0 (0.00%)	2 (0.38%)	0 (0.00%)	8 (1.69%)	1
Heart disease	10 (0.65%)	1 (0.33%)	0 (0.00%)	0 (0.00%)	8 (1.69%)	1
Labyrinthitis	9 (0.59%)	7 (2.31%)	1 (0.19%)	1 (1.41%)	0 (0.00%)	0
Infectious disease	7 (0.46%)	6 (1.98%)	0 (0.00%)	1 (1.41%)	0 (0.00%)	0
Metabolic	7 (0.46%)	1 (0.33%)	0 (0.00%)	0 (0.00%)	5 (1.06%)	1
Neurodegenerative disease	5 (0.33%)	1 (0.33%)	0 (0.00%)	0 (0.00%)	4 (0.85%)	0
Acoustic neuroma	4 (0.26%)	1 (0.33%)	0 (0.00%)	2 (2.82%)	1 (0.21%)	0
Vestibular Paroxysmia	1 (0.07%)	0 (0.00%)	1 (0.19%)	0 (0.00%)	0 (0.00%)	0
Others	110 (7.17%)	13 (4.29%)	10 (1.88%)	8 (11.27%)	67 (14.19%)	12
Unknown	692 (45.08%)	62 (20.46%)	239 (44.84%)	44 (61.97%)	228 (44.31%)	119
Total ¹⁾	1558	311	539	75	474	159

184 ¹⁾Since several diagnoses can be selected per case, there are more diagnoses than cases. For each diagnosis
 185 the corresponding syndrome is listed in the table, so the total number of the syndromes is higher.

186 Abbreviations: AVS (acute vestibular syndrome), EVS (episodic vestibular syndrome), CVS (chronic vestibular
187 syndrome), AIS (acute imbalance syndrome), BPPV (benign paroxysmal positional vertigo), TIA (transient
188 ischemic attack), PPPD (persistent postural-perceptual dizziness)

189

190 Accuracy of syndrome classification

191 662 (43.1%) out of 1535 patients received a follow-up. There was an excellent agreement (Cohen's
192 Kappa = 0,909, $p < 0.001$) between the syndrome classification at index visit and follow-up with a
193 reported change of the acute vestibular syndrome in 3.2% after the follow-up. Most of the misclassified
194 AVS patients were reassessed as EVS. EVS patients, however, were misclassified in 3.6%. Among
195 the patients with an AIS on the ED, the re-classification rate was 8.0%, whereas 1 patient was
196 subsequently classified as AVS. In the cases that could not be initially classified in the ED, 34.7%
197 could be classified as a vestibular syndrome or AIS in the follow-up examination (table 2).

198 **Table 2:** Cross tabulation - vestibular syndrome ED vs. follow-up (n=662)

		Follow-up						Change of syndrome [%]
		AVS	EVS	CVS	AIS	unclear	total	
ED	AVS	215	5	0	1	1	222	3.15%
	EVS	5	187	0	2	0	194	3.61%
	CVS	0	0	34	0	0	34	0.00%
	AIS	1	6	3	150	3	163	7.98%
	unclear	4	6	2	5	32	49	34.69%
	total	225	204	39	158	36	662	

199

200 Diagnostic errors in dizzy patients

201 In this section, we compare the diagnosis at ED with the diagnosis at follow-up (n=662). We report an
202 overall change in diagnosis between initial ED assessment and follow-up of 31.4 %. The proportion of
203 diagnostic errors (excluding patients with unknown causes) was 18.0%. There was a moderate to low
204 agreement between the initial diagnosis (ED diagnosis) and the final diagnosis after the follow-up
205 (Cohen's Kappa = 0.609, $p < 0.001$). Often diagnostic errors occurred in patients with dysautonomia
206 (33%, 6/9), TIA (30.6%, 15/49), BPPV (28.6%, 8/28), Menière's disease (26.7%, 4/15), stroke / minor
207 stroke (13.6%, 18/132) and for acute unilateral vestibulopathy (15.7%, 14/89). Of the cases with an
208 initial diagnosis of TIA, the diagnosis was changed during follow-up to "stroke/minor stroke" in seven

209 and to “unknown” in four cases (table 3 and additional file 1 table S1). The cause of the dizziness was
 210 at the time of the ED visit unknown in 37.6%. In 104 out of 662 cases the diagnosis remained unclear
 211 even after the follow-up exam, however, 58.2% of all unknown cases in the ED received finally a
 212 diagnosis and could be clarified (table 4). A special focus was placed on patients with an undiagnosed
 213 dangerous cause of dizziness (strokes / minor strokes, TIA) leading to potential diagnosis-related
 214 harm. There were two patients initially diagnosed with BBPV, three with acute unilateral vestibulopathy
 215 and one case with a medical side effect where the initial diagnosis was changed to TIA or a stroke /
 216 minor stroke at follow-up. Among patients with no specific diagnoses in the ED (classified as
 217 unknown/unclear), 14 patients had a stroke and 9 a TIA. In summary, in 29 of the 662 followed-up
 218 cases (4.4%) a dangerous diagnosis was found at follow-up (potential diagnosis-related harms) which
 219 was initially not diagnosed in the ED (see additional file 1 table S1, bold cases).

220 **Table 3:** Number of diagnostic errors, change of diagnosis rates, missed dangerous diagnoses and
 221 mimics.

ED Diagnoses	Total ED	# of diagnostic errors	Change of diagnosis*	# of missed strokes or TIA	Frequency of undiagnosed underlying diseases (top 3)**
Stroke / Minor stroke	132	18	13.6%	5 (TIA)	TIA (5) Acute unilateral vestibulopathy (4) Dysautonomia (1)
Acute unilateral vestibulopathy (e.g. Vestibular Neuritis)	89	14	15.7%	3	Stroke / Minor stroke (2) Menière (2) Others (2)
TIA	49	15	30.6%	7 (strokes)	Stroke / Minor stroke (7) BPPV (1) Metabolic (1) Medical side effects (1)
BPPV	28	8	28.6%	2	Acute unilateral vestibulopathy (3) Stroke / Minor stroke (2) Others (2)
Menière's disease	15	4	26.7%	0	Acute unilateral vestibulopathy (3) Labyrinthitis (1)
Tumor	14	1	7.1%	0	0
Vestibular migraine	12	3	25.0%	0	Others (2) PPPD (1)
Dysautonomia	9	3	33.3%	0	Others (2) Heart disease (2) Medical side effects (1)
Labyrinthitis	7	2	28.6%	0	Acute unilateral vestibulopathy (1) Acoustic neurinoma (1)

Infectious disease	6	3	50.0%	0	Acute unilateral vestibulopathy (3)
Heart disease	5	0	0.0%	0	0
PPPD	5	0	0.0%	0	0
Others***	42	4	9.5%	0	Dysautonomia (2) BPPV (1) Tumor (1)
Unknown	249	145	58.2%	23	Acute unilateral vestibulopathy (35) Vestibular migraine (22) Stroke / Minor stroke (14) TIA (9)
Total	662	222	31.4%	40	

222 *Since multiple answers were possible for the diagnoses, the number of diagnostic errors did not
223 necessarily correspond to the proportion of change of diagnosis. The rate of changes of diagnoses at
224 follow-up is calculated as follows: $100 * (1 - \text{correct diagnoses} / \text{total diagnoses ED})$.

225 **Undiagnosed underlying diseases: This column shows the most frequent changed diagnosis based
226 on the follow-up exam.

227 ***Diagnoses less frequent than five are not listed in the table.

228 **Table 4:** Unknown ED diagnoses resolved after follow-up

Diagnoses at Follow-up	unknown ED diagnoses (n=249)	Frequency
Acute unilateral vestibulopathy (e.g. Vestibular Neuritis)	35	14.06%
Others	28	11.24%
Vestibular migraine	22	8.84%
Stroke	14	5.62%
TIA	9	3.61%
Dysautonomia	8	3.21%
Menière's disease	8	3.21%
BPPV	6	2.41%
PPPD	6	2.41%
Unknown etiology central vestibular syndrome	4	1.61%
Metabolic disorders	3	1.20%
Tumor	1	0.40%
Medical side effects	1	0.40%
Heart disease	1	0.40%
Labyrinthitis	1	0.40%
Infectious disease	1	0.40%
Trauma	0	0.00%
Neurodegenerative disease	0	0.00%
Acoustic neuroma	0	0.00%
Unknown	104	41.77%

229

230 ED resource use

231 Overall, 69.9% of all 1535 dizzy patients received neuroimaging at the ED visit (MRI 58.2%, CT
 232 11.6%). 16.8% of stroke patients underwent a computed tomography (CT), 89.7% an MRI. Patients
 233 with a BPPV received in 41.3% an MRI and in 8% a CT showing a similar resource use as patients
 234 with acute unilateral vestibulopathy (48% MRI, 6.8% CT). Table 5 shows details of ED resource use
 235 stratified by ED diagnoses.

236 **Table 5:** ED Resources stratified by diseases (n=1535)

	Stroke / Minor Stroke	BPPV	Acute unilateral vestibulopathy	TIA	Menière's disease	PPPD	Trauma
MRI	139 (89.7%)	62 (41.3%)	71 (48.0%)	62 (80.5%)	11 (50.0%)	9 (40.9%)	3 (23.1%)
CT	26 (16.8%)	12 (8.0%)	10 (6.8%)	13 (16.9%)	0 (0.0%)	0 (0.0%)	6 (46.2%)
Audiology	5 (3.2%)	16 (10.7%)	90 (60.8%)	6 (7.8%)	12 (54.5%)	1 (4.5%)	0 (0.0%)
Caloric	8 (5.2%)	26 (17.3%)	115 (77.7%)	11 (14.3%)	9 (40.9%)	2 (9.1%)	0 (0.0%)
vHIT	4 (2.6%)	6 (4.0%)	41 (27.7%)	3 (3.9%)	2 (9.1%)	1 (4.5%)	0 (0.0%)
Total diagnoses	155	150	148	77	22	22	13

238 DISCUSSION

239 One fifth to one third of dizzy patients presented symptoms consisting of AVS or EVS. Another third of
 240 patients were not classifiable based on current criteria. Patients with CVS were noticeably less likely to
 241 present to the ED. In more than one third of the cases, which received a follow-up, the diagnosis was
 242 changed. Diagnostic uncertainty could be resolved at the follow-up visit in more than half of patients
 243 with unknown or unclear diagnosis. We found that a great number of imaging studies were ordered for
 244 dizziness workup.

245 Prevalence of vestibular syndromes and underlying diagnoses

246 The reported prevalence of AVS in the literature ranges from 10% to 22%, [2, 15] which matches our
 247 findings in the ED (20%). Our reported prevalence in the ED is not generalizable to other settings such
 248 as outpatient clinics, where the proportion of chronic vestibular syndromes might predominate. Violent
 249 vertigo attacks in patients with recurrent vertigo (EVS) might prompt patients to visit the ED rather than
 250 an outpatient clinic resulting in a high prevalence of 35%. The most common ED diagnoses in the total

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3 251 ED population were stroke / minor stroke, BPPV, and acute unilateral vestibulopathy, which is in
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5 252 agreement with other reports.[16,17] The posterior canal BPPV is the most common with 85-95% of
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7 253 BPPV cases. It can be diagnosed with the Dix-Hallpike maneuver which provokes a pathognomonic
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9 254 torsional upbeat nystagmus.[18] If spontaneous nystagmus is present, a diagnosis other than posterior
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11 255 BPPV should be considered and positional testing is not advised. The ED prevalence of strokes /
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13 256 minor stroke was 10% in our study, which is considerably higher than previously described (~4%
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15 257 cerebrovascular).[16,19,20] The reported prevalence, however is consistent with our previous,
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17 258 retrospective study from the same center with another sample.[21] In patients with AVS, however, the
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19 259 prevalence of stroke is significantly higher at 25.4% probably due to a referral bias of a tertiary care
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21 260 center including the largest stroke center of the country. Despite extensive investigations reflected in
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23 261 the resources used, almost half of the cases remained undiagnosed, which is higher compared to 22%
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25 262 in another cross-sectional study.[16] One reason for the higher number of “unknown” causes could be
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27 263 due to the applied classification rules classifying patients with multiple differential diagnoses as
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29 264 “unknown”.

30 265 **Accuracy of syndrome classification**

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33 266 Overall, the accuracy of the classification into three different vestibular syndromes was high. In one-
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35 267 tenth of the cases, the documented history was not sufficient to decide whether the patient had a
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37 268 vestibular syndrome. Possible reasons for this were a lack of documentation or an inappropriate
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39 269 history taking. In the group with a follow-up examination, more than one third of the unclear ED cases
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41 270 could be assigned to a vestibular syndrome or a vestibular syndrome could be excluded based on the
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43 271 extended history of the follow-up report. This finding emphasizes the importance of taking a targeted
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45 272 history (asking timing and triggers)[11,22] and the need of a follow-up to better assess the time course
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47 273 of dizziness. Digital decision support tools might assist physicians to take a structured and complete
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49 274 history. It is therefore important to improve digital competencies in the future.[23] Overall, there were
50
51 275 only a few misclassifications of vestibular syndromes in the ED. Misclassified EVS patients presenting
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53 276 initially as AVS had a short duration of symptoms which abated after the ED discharge. Diagnoses
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55 277 with EVS being at risk for misclassification as AVS included vestibular migraine, Menière’s disease
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57 278 and TIA. Main reason for misclassification was the first time occurrence of episodic dizziness with no
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59 279 previous history of dizzy episodes as mandated by international diagnostic criteria.[24,25] We also
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280 found misclassifications of AVS as EVS in patients with cerebral strokes, vestibular neuritis and with

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3 281 dysautonomia. Infarctions in the cerebellum (mainly PICA territory) can mimic positional vertigo,
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5 282 known as pseudo-BPPV.[26] Finally, each patient with an AVS suffers from motion intolerance, which
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7 283 can be misinterpreted as positional vertigo.
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11 12 285 **Diagnostic errors in dizziness patients**

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14 286 The terminology and definitions regarding diagnostic errors is under debate.[27] It can be used as an
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16 287 umbrella term including preventable, reducible or unavoidable diagnostic errors.[28] Our data,
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18 288 however, were not sufficient to assess the underlying diagnostic processes and workups leading to a
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20 289 specific diagnosis. We avoided, therefore, terms such as 'misdiagnosis', because such conclusions
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22 290 might be perceived as implicating errors in the diagnostic process, which we did not investigate. A sub
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24 291 classification into diagnostic process failure or diagnostic label failure was not possible based on our
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26 292 design. Diagnosing dizziness is a challenge for ED physicians and diagnostic errors are unavoidable
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28 293 even for experts in the field (following an optimal diagnostic process) due to the nature and complexity
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30 294 of the underlying diseases.[29] Thus, we aim to increase awareness about an unresolved issue
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32 295 regarding diagnostic accuracy in dizzy patients visiting the ED. In a German retrospective study, 124
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34 296 of 475 dizziness patients (26%) received follow-up.[17] This number is lower than the number of
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36 297 patients followed up in our study (43.1%). This selection bias has to be kept in mind, interpreting the
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38 298 presented results. The decision to schedule patients for follow-up could reflect an intimate uncertainty
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40 299 with the diagnosis or be an expression of increased caution of the treating physician with that
41
42 300 particular patient. In another study from our department on diagnostic errors the "feeling of atypical
43
44 301 presentation" was the only predictor of a diagnostic error.[30] This "feeling of atypical presentation" is
45
46 302 likely to prompt follow-up visits leading to a selection bias in our follow-up patients. We cannot exclude
47
48 303 any change in diagnosis within the observed period of 90days, however, the occurrence of a second
49
50 304 cause of dizziness unrelated to the initial diagnosis is very unlikely. In the German study, ED diagnosis
51
52 305 was corrected in 43%.[17] We observed a lower rate of diagnostic errors in our study (31%). Of the
53
54 306 benign ED diagnoses, 6% (n= 7 of 124) were finally diagnosed with a dangerous diagnosis during
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56 307 follow-up in the German study[17] compared to 4% (n= 29 of 662) in our study. Patients in our study,
57
58 308 however, received significantly more often MRIs in the ED (58% MRI vs. 18%). Another study reported
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60 309 a higher stroke misdiagnosis rate[20], however, ED physician misdiagnosis rate was based on
310 310 retrospective chart reviews derived from non-academic community hospital with limited access to

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3 311 neuroimaging and neurology expertise. This might contribute to the higher number of missed
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5 312 dangerous diagnoses (diagnosis related harm). Despite extensive ED workups in our study (including
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7 313 neuroimaging), four patients were still diagnosed as vestibular neuritis or BPPV and finally had a
8
9 314 stroke (Pseudo-neuritis or Pseudo-BPPV) without any focal neurological signs. Recent literature
10
11 315 confirms that 50% of patients with vestibular strokes might have isolated dizziness.[31,32] The MRI
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13 316 misses 10-20% of strokes presenting with AVS during the first 24-48h after onset.[33] Up to 50% false
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15 317 negative MRIs are reported for smaller vestibular strokes (<1cm).[31] The 'HINTS' examination can be
16
17 318 a possible solution for this dilemma. This three-step bedside exam, introduced in 2009,[34] includes
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19 319 the head impulse test, nystagmus test and test of skew and is more sensitive for stroke than early
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21 320 MRI. The application of a portable device using an eye-tracker and head accelerometers allows a
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23 321 quantitative and accurate stroke prediction in patients with AVS.[7,35-37] The comparison between
24
25 322 diagnoses at the index (ED) and the follow-up visit shows that in many cases a definite diagnosis can
26
27 323 only be made over time. This is often due to diagnostic criteria that require repetitive episodes of
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29 324 vertigo.[24,25] Some patients are symptom-free in the interval between episodes of dizziness or at the
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31 325 time of the emergency visit.

326 **ED resource use**

327 Altogether, neuroimaging was ordered in 70% of cases, of which 83% were MRIs. This high
328
329 percentage may be due to the 7/24-availability of MR imaging in our university hospital. We observed
330
331 that a large number of MRI was performed in patients who finally received a peripheral vestibular
332
333 diagnosis such as BPPV, Menière's disease or an acute unilateral vestibulopathy. The diagnosis of
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335 vestibular disorders can often be established by targeted history taking and clinical examination. There
336
337 is no need for neuroimaging in clinical diagnoses such as BPPV with a typical history and typical
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339 positional nystagmus elicited by diagnostic maneuvers.[38] Atypical findings (e.g. in BPPV with
340
apogeotropic nystagmus) or a diagnosis of exclusion (e.g. in Menière's disease) might still justify
neuroimaging (MRI) in the ED. CT scans, however, are only suggested in patients with suspected
trauma, hemorrhage or in patients with a contraindication for a MRI. The current clinical approach
leads to an unnecessary overuse of computed tomography and magnetic resonance imaging and
increases costs exceeding billions of dollars in the US alone.[39] Dizzy patients have longer average
ED stays than patients without dizziness because they undergo more testing.[16] The rate of
undiagnosed or misclassified patients remains high, resulting in higher costs and considerable waste

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2
3 341 of resources in the ED in Switzerland.[39–41] Furthermore, the overuse of computed tomography and
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5 342 magnetic resonance imaging may decrease access for other patients and it can increase the
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7 343 exposition to an unnecessary amount of radiation.

9 344 **Strengths and limitations**

11
12 345 The strengths of the study are the large number of included and screened cases and the
13
14 346 determination of vestibular syndromes based on history and follow-up assessments. A more accurate
15
16 347 classification into the vestibular syndromes would need, however, a prospective longitudinal study
17
18 348 design. We also observed a referral bias (tertiary referral center) leading to a higher proportion of
19
20 349 dangerous diagnoses in dizzy patients. In addition, the treating clinician decided whether a follow-up
21
22 350 was pursued, which may have caused a selection bias.

24 351 **Implications for clinicians**

26
27 352 Our study confirms that about a fifth of patients suffers from AVS. The high prevalence of strokes in
28
29 353 patients with continuous dizziness (25%), the high number of undiagnosed or misclassified cases
30
31 354 should increase the overall awareness regarding diagnostic errors and stroke mimics. Consequently,
32
33 355 we suggest a three-stage diagnostic test process for patients presenting with dizziness in the ED. This
34
35 356 approach does intend increase diagnostic accuracy and to reduce neuroimaging in the acute stage.
36
37 357 We suggest, therefore,

38
39 358 1) A more sensitive screening (triage) test including a classification into vestibular syndromes
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41 359 (targeted history) and recording of spontaneous nystagmus, 2) a targeted clinical exam with either
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43 360 “HINTS” test[34] in AVS patients or “Dix-Hallpike” examination[38] in EVS patients with triggers and 3)
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45 361 a dedicated neuroimaging (e.g. acute and delayed MRI) in patients with suspected central causes of
46
47 362 vertigo. Furthermore, additional tests such as the Bucket Test[42] or stance and gait tests (searching
48
49 363 for truncal ataxia)[43] can further increase the sensitivity for the detection of stroke patients.

50
51 364 In patients with EVS and absence of triggers (suspected Menière’s disease or vestibular migraine) we
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53 365 alternatively suggest as a second stage caloric testing and audiometry in a planned follow-up and as a
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55 366 third stage a delayed neuroimaging (diagnosis of exclusion). Patients without any nystagmus
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57 367 (spontaneous or after provocation) might need a more extended neurological exam such as BE-
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59 368 FAST.[44] Patients with inconclusive or atypical findings might need further assessment for risk factors
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369 (e.g. ABCD2 score)[45] in order to minimize the risk for missed minor strokes and to prevent future

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3 370 harmful events. We further recommend a low threshold for organizing a follow-up appointment in dizzy
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5 371 patients since the symptoms and the diagnosis might change over time. This study paves the way for
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7 372 future studies providing epidemiological data including the expected prevalence for each type of
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9 373 vestibular syndrome.

10 11 374 **CONCLUSION**

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13
14 375 One fifth of dizzy patients in the ED presented with AVS with a high prevalence (10%) of vestibular
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16 376 strokes. Episodic vertigo (EVS) was more frequent, however, the rate of undiagnosed dizzy patients
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18 377 and the number of patients receiving neuroimaging was high. Almost half of them still remained
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20 378 without diagnosis and among those diagnosed were often misclassified. Many unclear cases of vertigo
21
22 379 could be diagnostically clarified after a follow-up visit.

23 380

24 381

25 382

26 383 **ABBREVIATIONS**

27 384 ED emergency department

28 385 AVS acute vestibular syndrome

29 386 EVS episodic vestibular syndrome

30 387 AIS acute imbalance syndrome

31 388 CVS chronic vestibular syndrome

32 389 TIA transient ischemic attack

33 390 BPPV benign paroxysmal positional vertigo

34 391 AUVP acute unilateral vestibulopathy

35 392 MRI magnetic resonance imaging

36 393 CT computer tomography

37 394 vHIT video head impulse test

38 395 PPPD persistent postural-perceptual dizziness

39 396 VOG video-oculography

40 397

41 398 **DECLARATIONS**

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2
3 399 **Ethics approval and consent to participate:** The study was approved by the local ethics committee
4
5 400 (KEK Bern, #2021-00918). Given the retrospective nature of the study, informed consent was provided
6
7 401 through a hospital-wide general consent. Patients who withdrew consent for evaluation of their medical
8
9 402 data were excluded in accordance with legal requirements.

10
11 403 **Consent for publication:** Not applicable

12
13 404 **Availability of data and materials:** The datasets used and/or analyzed during the current study are
14
15 405 available from the corresponding author on reasonable request.

16
17 406 **Competing interests:** None of the investigators has any relevant financial interests, activities,
18
19 407 relationships, or affiliations that represent a relevant financial conflict of interest with respect to the
20
21 408 conduct or analysis of this study.

22
23
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25
26 410 **Authors' contributions:** AK, EZ, FN and LC collected and processed the data. GM and LC conceived
27
28 411 the study, analyzed and interpreted the data and wrote the draft. MC, TS, FW and SJ were involved in
29
30 412 the interpretation of the data and in the review. All authors discussed the results, commented on the
31
32 413 manuscript, and read and approved the final version.

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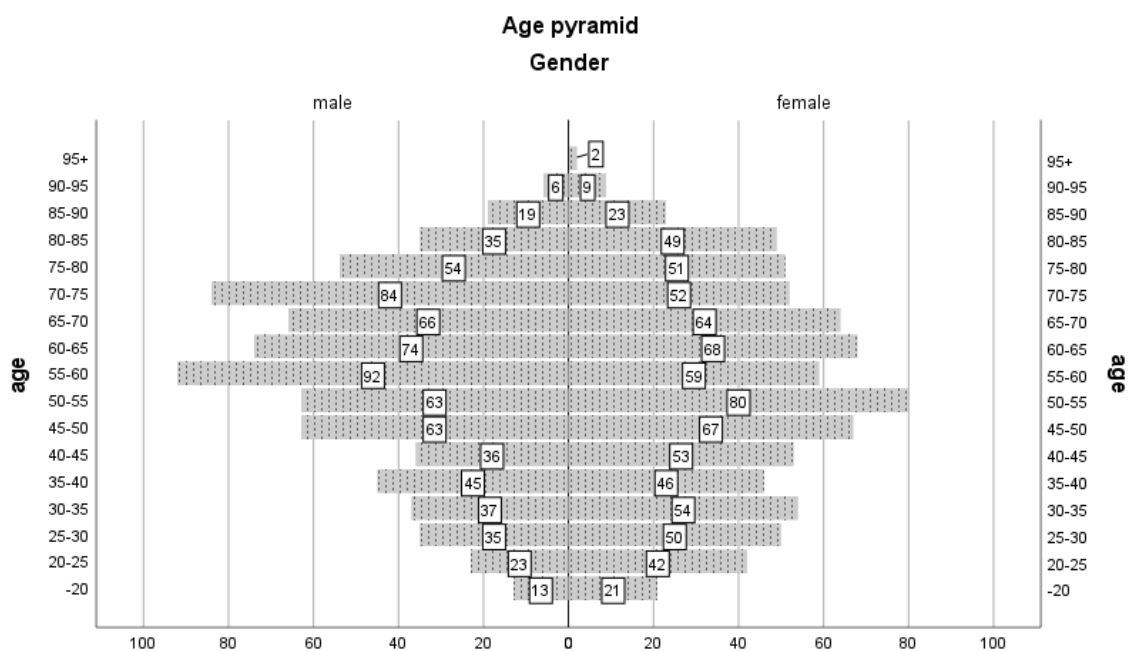
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Vestibular syndromes, diagnosis and diagnostic errors in dizzy patients presenting to the emergency department. (Comolli et al.)

APPENDIX

Figure S1



review only

Frequencies of vestibular syndromes, diagnosis and misdiagnosis rates in a tertiary emergency department (Comolli et al.)

Table S1: Cross table diagnoses emergency department (ED) vs. Follow-up

Bold cases represent the 29/662 (4.4%) cases where a dangerous diagnosis was found during follow-up but not during ED workup

	Diagnoses follow up																				Change of diagnoses at follow-up ²⁾	
	Stroke / Minor Stroke	BPPV	Vestibular Deficit (e.g. Vestibular Neuritis)	TIA	Dysautonomia	Vestibular migraine	Menière's disease	PPPD	Tumor	Trauma	Medical side effects	Heart disease	Labyrinthitis	Infectious disease	Metabolic disorders	Neurodegenerative disease	Acoustic neuroma	Others	unknown	unknown etiology central vestibular syndrome		Total Diagnoses ED ¹⁾
Stroke / Minor Stroke	114	0	4	5	1	0	0	0	0	0	0	0	0	0	0	0	0	1	4	3	132	13.6%
BPPV	2	20	3	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2	2	0	28	28.6%
Vestibular Deficit (e.g. Vestibular Neuritis)	2	0	75	1	0	1	2	0	0	0	0	0	1	0	0	1	1	2	6	0	89	15.7%
TIA	7	1	0	34	0	0	0	0	0	0	1	0	0	0	1	0	0	0	4	1	49	30.6%
Dysautonomia	0	0	0	0	6	0	0	0	0	0	1	2	0	0	0	0	0	2	0	0	9	33.3%
Vestibular migraine	0	0	0	0	0	9	0	1	0	0	0	0	0	0	0	0	0	2	1	0	12	25.0%
Menière's disease	0	0	3	0	0	0	11	0	0	0	0	0	1	0	0	0	0	1	0	0	15	26.7%
PPPD	0	0	0	0	0	1	0	5	0	0	0	0	0	0	0	0	0	0	0	0	5	0.0%
Tumor	0	0	0	0	0	0	0	0	13	0	0	0	0	0	0	0	0	0	1	0	14	7.1%
Trauma	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	3	0.0%
Medical side effects	1	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	3	33.3%
Heart disease	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0	5	0.0%
Labyrinthitis	0	0	1	0	0	0	0	0	0	0	0	0	5	3	0	0	1	0	0	0	7	28.6%
Infectious disease	0	0	3	0	0	0	0	0	0	0	0	0	1	3	0	0	0	0	0	0	6	50.0%
Metabolic disorders	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0.0%
Neurodegenerative disease	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	1	0	0	3	33.3%
Acoustic neuroma	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	4	0	0	0	4	0.0%
Others	0	1	0	0	2	0	0	0	1	0	0	0	0	0	0	0	0	38	1	0	42	9.5%
unknown	14	6	35	9	8	22	8	6	1	0	1	1	1	1	3	0	0	28	104	4	249	58.2%
Total Diagnoses Follow up ¹⁾	138	28	122	49	17	32	21	11	15	3	4	8	9	5	5	3	5	73	122	8	662	

¹⁾The fields "total" refer to the number of the corresponding diagnosis. Since several diagnoses are possible, the columns and rows do not add up.

²⁾ The rate of changes of diagnoses at follow-up is calculated as follows: $100 * (1 - \text{correct diagnoses (grey fields)} / \text{total diagnoses ED})$

BPPV = benign paroxysmal positional vertigo; TIA= transient ischemic attack; PPPD = persistent postural-perceptual dizziness

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3/4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(b) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6
		(b) Describe any methods used to examine subgroups and interactions	6
		(c) Explain how missing data were addressed	5/6
		(d) If applicable, explain how loss to follow-up was addressed	not applicable
		(e) Describe any sensitivity analyses	not applicable
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6/7
		(b) Give reasons for non-participation at each stage	16
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6-11
		(c) Summarise follow-up time (eg, average and total amount)	7/8
Outcome data	15*	Report numbers of outcome events or summary measures over time	6-11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	not applicable
		(b) Report category boundaries when continuous variables were categorized	not applicable
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-15
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.