Chapter

Sleep and the Fitness to Drive: A Swiss Perspective

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Abstract

Medical conditions and behavioral patterns affecting sleep are a largely underestimated threat to traffic safety. Unsupervised or even illegal self-treatment of sleep issues by, for example, anti-histamines, cannabis products, or stimulants, questions safe driving and the fitness to drive as well as low compliance/adherence to treatments (CPAP, medication, etc.) of medical conditions, such as OSAS, or narcolepsy. In such cases, Swiss law calls for a medical assessment of the fitness to drive by experts in traffic medicine. With increasing complexity, this medical assessment is escalated in a four-tiered system of qualified experts, ranging from a qualified practitioner to experts in traffic medicine, at, for example, an Institute for Legal Medicine. The following overview provides insight in the Swiss framework of traffic medicine assessments that – with all caveats and potential drawbacks – helps mitigating the risk of sleep-related accidents. For this, we first introduce Swiss traffic medicine and then argue for consistent terms and measurements to assess sleepy driving. A concise summary of those sleep related conditions most relevant in traffic medicine is followed by an overview over potential issues of sleep-medication.

Keywords: sleep, fitness to drive, traffic medicine, OSAS, narcolepsy, sleep medication

1. Introduction

The consequences of medical conditions and behavioral patterns negatively affecting sleep pose a largely underestimated threat to traffic safety. According to a recent survey of Swiss road safety authorities (ASTRA), about 2% of all car accidents in Switzerland are documented to be caused unequivocally by the driver falling asleep [1]. Similar numbers are reported from other countries. The U.S. Institute for Insurance Information (III) lists "drowsy, asleep, fatigued, ill or blacked out" operation in 2.4% of drivers/operators involved in fatal crashes [2] and the U.S. National Highway Traffic Safety Administration (NHSTA) reports 1.9% of fatalities in motor vehicle crashes to have involved drowsy driving [3].

However, the estimated number of undetected or unreported accidents and fatalities might be much higher: various sources suspect that up to 30% of all accidents can be related – in part or full – to either falling asleep or to sleepiness at the wheel [4–6]. A study commissioned by the Australian Sleep Health foundation [7] and summarized prevalence and prevention information by the U.S. Center for Disease Control (CDC) [8] indicate that a surprisingly large fraction of the

respective population suffers from undiagnosed sleep deprivation. In a representative poll, 1 in 25 U.S. adult drivers (ages 18 or older) report to have fallen asleep while driving in the last 30 days [9]. The NHSTA estimates that drowsy driving was responsible for 72,000 crashes, 44,000 injuries, and 800 deaths in 2013. These numbers are likely underestimated, and up to 6,000 fatal crashes each year may be caused by drowsy drivers in the U.S. alone [8, 10–12].

While the two preceding paragraphs illustrate the scope (of the threat/risk/challenge) with (impressive) figures, they also highlight a fundamental problem for mitigation strategies and concepts, i.e. an apparently incomplete definition and demarcation of terms used above, such as "drowsy, asleep, fatigued, ill, [...] blacked out" [2], unconscious, tired, sleep-deprived or sleepy. The large spectrum of terms in use is in contrast to the need of a medical expert to communicated clearly and in a specific manner, not only with peers, but also in court, in assessments for authorities issuing driving licenses, and – last but not least – with his patients.

To briefly provide a few – possibly trivial, but illustrative – examples: it is essential if an unconscious patient caused an accident because he fell asleep or due a "black-out" (transient loss of consciousness, TLoC). Similarly, it is important whether a driver reports a "permanent subjective feeling of tiredness", or lacks any pre-sensation of spontaneously falling asleep in irregular intervals. While the latter might indicate narcolepsy, the first might possibly be very distracting from and dangerous for driving (inattention), but it might be short of any measurable danger to actually fall asleep. Chronic sleep-deprivation or sleep-fragmentation might lead to clearly measurable daytime sleepiness (excessive daytime sleepiness, EDS), but this might remain completely unnoticed to the driver. Over time, the driver's might have lost the ability to distinguish sleepiness from a (transient morning-) drowsiness or a post-prandial fatigue might have eroded, irrespective of the causes.

In the best case, any of the above conditions or situations is known ahead of any incident and family practitioners and experts in sleep- and traffic medicine collaborate for the best possible treatment and control to prevent any (daytime) sleepiness, in particular while driving.

However, one or more of the above situations or conditions might remain undetected, resulting, in the worst case, in an accident truly caused by the driver actually falling asleep. Such accidents, briefly termed sleep accident (SA) in the following text, usually exhibit certain characteristics. Drivers crash on a well-known monotonous road stretch, close to the final destination (e.g. home or work). Typically, there are no detectable traces of braking, of avoiding obstacles/vehicles or of abrupt changes in direction. In addition, drivers are usually well oriented and responsive in a clear and alert manner immediately following the accident [13]. However, indications are not always as clear and it is the second very mandate of traffic medicine to identify and document the causes of such accidents *post hoc*.

As already seen before, reasons for (daytime) sleepiness can be numerous and divers. Statistical figures hint at how one could structure a description of causes on a first level: the predominant fraction of SAs of drivers under 40 happen in weekend nights. In contrast, sleep accidents of drivers above 40 happen mostly on weekdays in the (late) afternoon [4]. Thus, following a dichotomization in "the younger partying" and "the older suffering from xx", the reasons can be divided very coarsely in predominantly behavioral or medical.

On a second level, the first might be further detailed in behavioral, social, professional and environmental reasons, whereas the latter might stem from central, neurological, somatic or psychiatric conditions or, finally, be substance- or medication-induced (See Table 5 in Chapter 3).

On a third level, that is also important for an overall assessment in traffic medicine, behavioral and social patterns overlaying fundamental causes might

Signs of sleep accident	**Signs of TLoC-accidents**
Monotonous, well known route	—
Close to destination	—
No trace of breaking	No trace of breaking
Immediately oriented driver	Continued disorientation
Diffuse knowledge about falling asleep	Despair about unclarity of causes
Rather trying to obscure clarifications	Strong interest in clarifying causes
Drivers aged <40: rather weekend nights	Independent of age
Drivers aged >40: rather afternoons	Independent of age
Seen by other drivers	**Seen by other drivers**
Slow reduction in speed	Abrupt changes in direction
Slowly loosing track	

Table 1.
Comparison of characteristic signs of sleep accidents as compared to accidents caused by a transient loss of consciousness (TLoC).

further aggravated the sleep conditions and associated risks in traffic. Especially in affluent and highly developed countries, with dense traffic and high social stress, sleep conditions are often counteracted by excessive use of commercially available stimulants (caffeine) or over the counter (OTC) substances (melatonin, doxylamine, diphenhydramine). Rather than addressing the problem, masking it by (an often inappropriate) use of such remedies already hampers mitigation of the risks. At the same time, several rounds of "next generation" sleep medication have repeatedly shown to involve the danger of developing tolerances, rebound- or side-effects, and even addiction. Especially latter is relevant in the context of self-medication and off label use of prescribed medication (antidepressants) or even drug abuse (cannabis, upper/downer, and opioids [14]), potentially causing unpredictable drug interactions leading to sudden sleepiness or TLoCs (**Table 1**).

The preceding paragraphs already outline the overall structure of the chapter and briefly sketch order and content of its sections: First, we introduce the unique set-up of Swiss traffic medicine, some necessary legal terms and recent organizational developments. We then argue for consistent use of terms and measurements used in the assessment of sleepiness. Following is a brief overview over those sleep conditions most relevant in every-day traffic medicine, including respective treatment options that are relevant to follow-up assessment. Lastly, we illustrate dangers of uninformed or inappropriate use of hypnotics and antidepressants due to drug interactions, highlighting the particular power of hair-analysis.

The chapter mostly collects regulations and existing literature. However, it is supplemented with two case reports and a short report on case numbers from the database of the division of traffic medicine at the Institute of Forensic Medicine at the University of Zurich.

2. Traffic medicine in Switzerland

To mitigate risks in traffic in general, Swiss license holders have to fulfill medical minimum requirements (MMR) by law (Strassenverkehrsgesetz, SVG Art 14 & 15 d, and Verkehrszulassungsverordnung, VZV, Art 7 [15, 16]). Swiss legislation already defined these "medical minimum requirements "(MMR) in 1932 in the form

of ordinances [17]. These MMRs have been continuously modernized and adapted. In addition, they are framed by detailed subject-specific guidelines.

It is thus surprising that – despite known fatalities due to sleep accidents, the MMRs did, in fact, lack any explicit requirements with respect to sleep until 2016. Only then, a revision of the VZV in the context of a large-scale legislative effort to modernize and improve traffic (Via Sicura) specified in the MMR that there must not be any diseases or conditions leading to "elevated" daytime sleepiness. However, who does determine whether such a condition is or was present, and how? Are other contributing factors evaluated?

In general, the medical minimum requirements are controlled by experts trained in traffic medicine, who are organized and trained in a four-tiered federation-wide system, ranging from a trained physician (level 1) to full time experts (level 4, see **Figure 1**) since 2016.

Within this system, the medical assessment is escalated depending on the category of driving license applied for or increasing complexity, allowing for second opinions in doubt up to a level-4 expert, who are mostly associated with institutes for forensic/legal medicine. Among others, the law requires mandatory biannual checkups of elder drivers above age 75 for all categories and mandatory control exams for higher categories, such as professional taxi-, bus- or truck-drivers, after 3–5 years.

In the context of a sleep accident, the driver is in any case confronted with the question whether falling asleep – and thus the accident – happened in negligence; in other words, did the driver's behavior or wrongdoing lead to falling asleep or can it be attributed to a known or unknown medical condition. Apart from clarifying the legal issue of liability, this has direct consequences on the driver's license, as there are - at least – justified doubts whether the driver can fulfill the MMRs. In Swiss legal terms, it needs to be clarified whether the drivers momentary ability to drive (ATD, German: Fahrfähigkeit) or the drivers general fitness to drive (FTD, German: Fahreignung) was/or is given.

The legal term ability to drive (ATD,) refers to the driver's momentary and incidental physical and mental capabilities to safely conduct a vehicle. The ability to drive safely can be impaired by, for example, alcohol, improperly used medication and/or drugs. In addition, Swiss Federal Court rulings elaborate that in order for a driver to be legally "able to drive", both a basic capability and a mental and behavioral reserve capacity is required. This reflects the need to be able react adequately

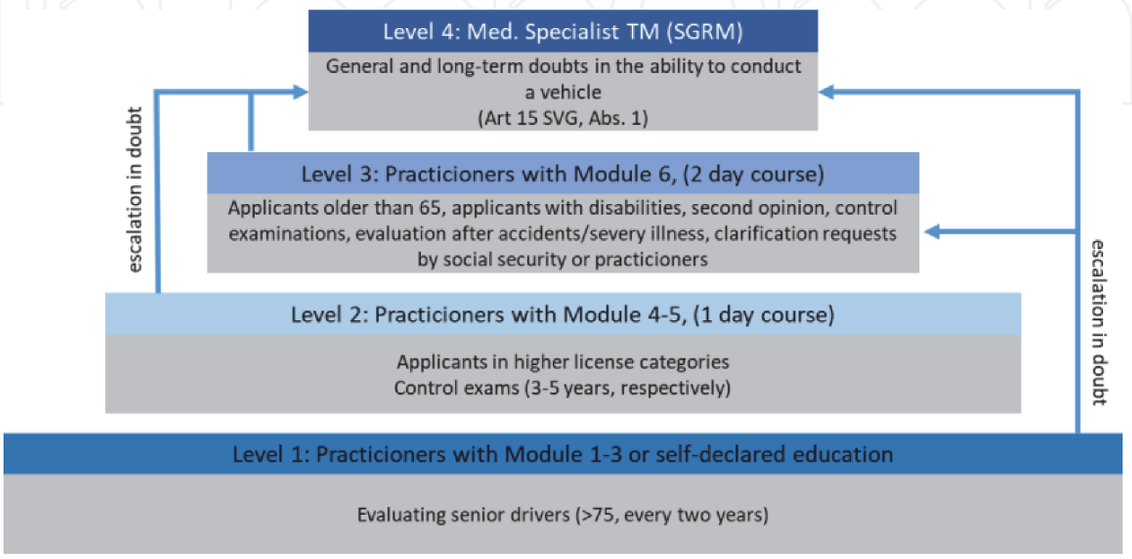

Figure 1.
Swiss four-tiered system of experts trained in traffic medicine.

to unexpected incidences in traffic and thus refers to the driver's requirement to guarantee this capacity before while driving, i.e. behavioral aspects, habits or character.

In contrast, the legal term "fitness to drive" (FTD) refers to the general physical and mental prerequisites to safely conduct a vehicle, unrelated to a specific incident or moment, relating obviously to chronic medical conditions limiting driving, which is in conflict with the MMRs. An assessment of the FTD or ATD at the level 3 or 4 generally encompasses a cursory medical examination (traffic medical exam, TME), anamnesis the patient's general medical status, history and recent incidents/events. Simple cognitive performance tests (mini mental status tests, clock test, trail making tests) reflect the need to take into account the general performance capabilities (German: Leistungsfähigkeit), assuming that safe driving requires both a basic physical and mental capacity (for undisturbed traffic, German: Grundleistung) as well as a mental and physical reserve capacity, relevant in unforeseen situations (German: Reserveleistung) [18].

While lower level assessments formally check general health, compliance, and adherence of, for example, the elderly drivers as required in two-year intervals at ages 75 and higher, higher-level assessments clearly deal with substantial doubts in the FTD, including those doubts relating to signs of addictive behavior and drug abuse. The final assessment provide the decision base for the authorities issuing the driving license.

According to recently updated guidelines [19], not all drivers who have caused a presumed sleep accident have to undergo a full TME and TMA in a top-tier institution (level 4): it is mandatory if there is information or hints pointing at either a medical condition or medication as the cause for falling asleep. In this case, the driving license is temporarily revoked until the authorities further decide based on the TMA. This is also the case, if it is unclear to both the driver and/or the authorities, whether the accident was truly caused by falling asleep or a transient loss of consciousness (TLoC, see Section 2.1) [20]. In case the driver can plausibly explain the accident by falling asleep due to behavior (too little sleep, shift work, etc.), a TMA is not required and subsequent sanctions by the authorities rely fully on the concession of an impaired driving ability.

2.1 Transient loss of consciousness as "camouflage statement" in sleep accidents

Because a first-time TLoC based on a so far unknown medical condition is presumed to have positive effects on the driver's liability assessment, a TLoC is often stated to "camouflage" any form misbehavior [21]. This is understandable in the context of patients that are, for example, very well aware of their own low medical or behavioral compliance/adherence, with known preconditions or psychogenic and gar-related cognitive deficits. Here, shame and the fear of consequences need to be taken into account.

A transient loss of consciousness (TLoC) as cause of an accident is already highly unlikely if during the anamnesis of the accident situation the above-mentioned characteristics can be found. However, this needs to be delimitated clearly; TLoCs can be caused by cerebral hypo-perfusion of cardiac, orthostatic or reflex origin, such as syncope, functional and medication arrhythmia, hypotonia, vasovagal reflexes hyper-responsive baroreceptor reflex in the carotid sinus or – without cerebral hypo-perfusion – by neurological, pharmacological or endocrinology conditions, such as epilepsy, narcolepsy, intoxication, hypoglycemia. In addition, a TLoC needs to be delimitated from other conditions such as a psychogenic

pseudo-syncope, catatonia or cataplexy. The latter is often associated with narcolepsy and – in accident reconstruction – easily confused with falling asleep.

3. Sleepy driving: terms and measurements

The following section intends to take up the point of "incomplete definition and demarcation of terms used" as described in the introduction and tries to link a clarification to the legally binding - albeit slightly unclear - term "elevated daytime sleepiness" from the MMRs in Section 2, by arguing for ideally using consistent terms and measurements.

With "elevated daytime sleepiness" being the central term in Swiss legislation, this section, thus, clarifies our understanding of a.) Sleepiness (What are the signs of Sleepiness? What is sleepy? What is daytime sleepiness?) and b.) how to appropriately measure it? What is "elevated", "excessive" ... or – for that matter – "existing" (measurable) daytime sleepiness?

3.1 Sings of sleepiness

Fundamentally and independent of the time of day, measurement condition or cause, the state of "sleepy" displays unequivocal sings of imminent falling asleep. If the sleep needed is avoided - either willfully or by external force - these sings increase in frequency: if one is "sleepy", one yawns often and attack-like. Furthermore, it is increasingly difficult to keep the eyes open and these are often felt as "dry" and heavy ("heavy eyelids"). Muscle-tone and attention decrease significantly. Vision is reduced in focus and perception speed, often leading to blurred or even doubling pictures. In consequence, it becomes difficult to integrate environmental input correctly and to react to them in timely manner. At the same time, continued monotonous activities become erratic and concentrated. Sleepy test subjects also report on changed temperature sensation (rather towards chilly) and slightly increased perspiration (**Table 2**).

All these signs are believed to be noticed by all drivers [22, 23] well before influencing the driving performance significantly [24]. However, it remains unclear if, for example, chronically sleepy individuals (such as shift workers, truck drivers, etc.) are still able to correctly judge these signs and/or act accordingly. This might be influenced by continued willful ignorance and, thus, familiarization/desensibilisation.

As mentioned above, there exists a general uncertainty as to how discriminate the state of "sleepiness" from terms that are used in a similar or even synonymous way: these include tiredness, exhaustion and drowsiness (see below). Lastly, the difficulty to actually "measure" and "communicate a measure" of sleepiness should not be underestimated, even in the medical and diagnostic context. Therefore, the following section aims at clarifying terms and measures used in Swiss traffic medicine.

3.2 Measures of sleepiness and its relevance in traffic medicine

As clarified in the preceding section, sleepiness *per se* is a natural reaction: it is the direct presage of the functional and unavoidable necessity to sleep, as dictated by chronobiology in (more or less) regular intervals, normally in the evening [23, 25, 26]. Therefore and irrespective of the cause, be it medical or behavioral, the customary composite "day-time sleepiness" describes an unusual and, in traffic, inacceptable condition.

Signs of sleepiness
Yawning (repeated, in attacks)
Dry eyes
«heavy eye lids
Sharp vision requires effort
Reduced muscle tone
Reduced attention, effort for vigilance strongly increased
Changed temperature sensation
Sweating (forehead)
Consequences for perception and performance in general
Visual perception slowed down and blurred
Slowed and error prone integration of environmental influences
Monotonous actions/tasks increasingly erratic and unconcentrated
Effects on driving performance
Track and speed cannot be held constant
Unexpected reduction of speed, inexplicable for others
Abrupt corrections of speed and direction when waking up

Table 2.
Unequivocal signs of being sleepy at the wheel.

Independent of the time of day, "sleepiness" also describes an initially abstract measure of the inclination or tendency to fall asleep [27]. Transferred in a concrete and manageable measurement, this measure is operationally defined as the recorded time from a test start until a test subject actually falls asleep (in minutes), i.e. a latency. This parameter is also termed "sleep latency", but requires the actual test situation to be named (see below). Although seemingly intuitive, but slightly incorrectly, this parameter is also circumscribed as "sleep propensity" (**Figure 2**).

Figure 2(a) displays a schematic course of performance change during the day in % (after [23]). Based on this, **Figure 2(b)** illustrates the measurement of sleep latencies and allows clarifying the difference between the terms sleep latency and sleep propensity (sleep inclination). Solid lines in red or blue, respectively, illustrate schematically the "course" (on an arbitrary, qualitative scale ranging from "awake" to "asleep") from the start of the test (t = 0) until the test subject has fallen asleep (crossing the x-axis). L1-L3 indicate three different sleep latencies. It is apparent that on red and blue solid lines each result in the same sleep latency, but starting from a different (abstract and qualitative) activity level. The dashed red and blue lines, four of which are denoted as N1-N4, indicate the slopes (inclinations) resulting from start and end of the measurements. N1-N4 help to illustrate the slightly misleading term sleep propensity/inclination: given the same latency L1, N1 shows a steep slope, N2 displays a flat slope, as it starts form a lower activity level. N2 is similar to N3, which relates to a much longer latency L3. Vice versa, N4 is much smaller as compared to N3 although it corresponds to the same Latency L3. As the latency has been made accessible through operationalization, the activity level remains fully elusive. Consequently, the terms sleep inclination/propensity should be avoided in favor of the clearly defined sleep latency. The same applies to terms such as sleep pressure for which an illustrative correlate is even harder to find.

Sleep latencies are usually measured in two ways, the MSLT and the MWT [28]. Most frequent in sleep medicine is the classical multiple sleep latency test (MSLT).

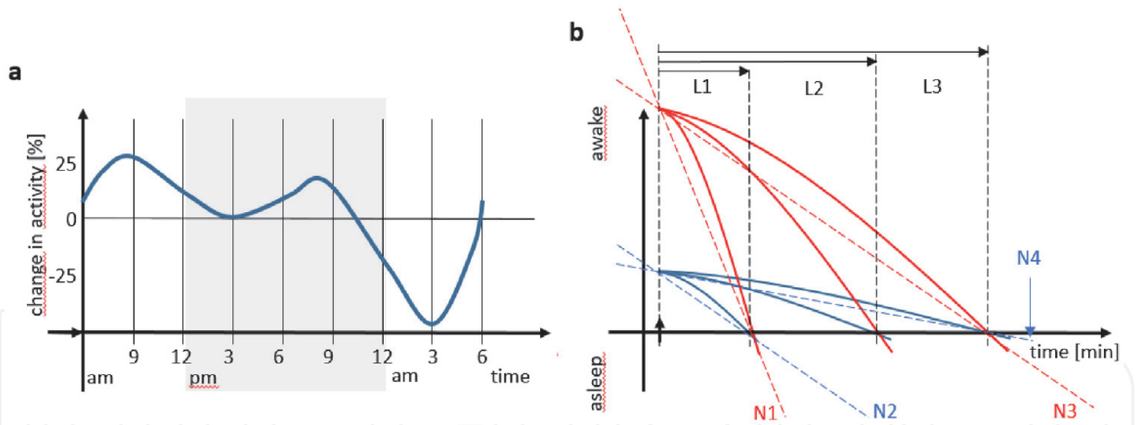

Figure 2.
(a) Schematic course of performance change during the day in % (after [23]). (b) Three exemplary courses of activity from awake to asleep form two different starting levels (red and blue) including measured sleep latencies (L1–L3, black arrows)). N1–4 (red and blue dashed lines) illustrate slopes (inclinations) to argue against the terms sleep inclination or sleep propensity (see main text).

In four or five repetitions at intervals of 2 h, it is observed, if - and how fast - a test subject is falling asleep within 20 min. Individuals are subjected to a typical sleep setting: she/he is lying in a bed in a fully darkened room with closed eyes and with the purpose to fall asleep. Once the EEG registers a > 15 s stretch of one or more of the three typical sleep states, the measurement stops and the individual is woken up. Final MSLT sleep latency is the average of the 4–5 measurements. The MSLT thus measures how fast a test subject can manage to fall asleep during the day.

The multiple wakefulness test (MWT) measures also a sleep latency, but approaches sleepiness from the opposite perspective, i.e. the wish to stay awake. Individuals are subjected to a soporific, but not ideal situation: she/he is sitting in a comfortable chair in a partially darkened (dim) room with open eyes and with the clear purpose not to fall asleep, i.e. to stay awake. Again, the above-mentioned 15 s-rule for the EEG applies to determine after how long an individual has fallen asleep within either 20 min. or - more usual - 40 min. Again, this latency is measured in four or five repetitions with intervals of 2 h. Final MWT sleep latency is the average of the 4–5 measurements. The MWT thus measures, how many minutes a person can (actively) avoid falling asleep during the day. The MWT includes active elements and incorporates the ability of the test subject to counteract falling asleep. Consequently, the MWT is considered more comparable to assessing a driving situation than the MSLT [28, 29].

However, clinicians might use definitions of EDS and criteria of it in MWT/MSLT differing from or overlapping with those in traffic medicine [28]. The new ICSD-3 [30, 31] defines EDS as “daily episodes of an irrepressible need to sleep or daytime lapses into sleep”. For disorders, such as narcolepsy and idiopathic hypersomnia (IH), which require demonstration of objective sleepiness by the multiple sleep latency test (MSLT), a mean sleep latency of 8 min on the MSLT is required. This criterion is unchanged from the ICSD-2 and represents the best compromise between sensitivity and specificity [32]. Here, the MWT is not specifically mentioned as diagnostic tool, while its relevance in the clinic has been proven useful for the evaluation of treatment success with respect to everyday life situations [28].

Swiss guidelines for traffic medical assessments allow for a modification of the MWT, in slight favor of the drivers, the FTD-MWT: here is allowed to consume usual amounts of beverages containing caffeine during breaks and to take one midday nap of 20 min. Both is not allowed in the diagnostic classical MSLT and MWT. In practice, the number of modified FDT-MWTs is, however, very low.

In order to discriminated daytime sleepiness as measured predominantly by MWTs from an increased demand of sleep due to neurological conditions, such as a hypersomnia or a narcolepsy [28], the MWT is usually accompanied by polysomnography (PSG, classic, ad libitum) which should ideally follow directly after a 14-day period of actigraphy, including protocolling the sleep behavior [29].

Such "objective" measures of sleepiness as measured in MWT or MSLT should be clearly distinguished from phenomenological experienced and questionnaire-based, i.e. "subjective" sleepiness. Some questionnaires and methods (KSS, as well as VAS-batteries), determined a "momentary and felt" sleepiness, whereas, for example, the ESS determines the subjective estimate of sleepiness over a period of time (usually 14 days) post hoc and in relation to representative situations and, therefore, registers - at best - an average subjective feeling. Although often in use, the ESS is strongly criticized for is high level of subjectivity [27]. Also, the ESS offers low prognostic reliability, as the subjective estimate of sleepiness might manifest differently in different, soporific situations, such as monotonous night drives or similar [33].

3.3 Day-time sleepiness: qualifiers and guidelines

It is the very nature of the so-far mentioned tests that, in principle, they can measure both the natural sleepiness induced by medical conditions and behavioral patterns, both in the course of the day and at night. *In realiter*, these tests are almost exclusively performed and related to the common daytime period, in order to evaluate deviation from the norm.

Intermittent or chronic sleepiness during the day as measured by way of above-mentioned objective methods is termed "daytime sleepiness". However, in different contexts the term is often complemented with varying qualifying adjectives: to state two, the medical field generally prefers the term "excessive daytime sleepiness" (EDS) [34] mostly in connection with insomnias and other conditions. As introduced in Section 2, Swiss law prohibits driving with medical conditions leading to any "elevated" (German: erhöhte) daytime sleepiness. Other qualifiers "significantly increased", "relevant", "excessive" and "severe" daytime sleepiness, leaving the reader often without respective information how to understand and value the qualifier. German regulations have taken up this issue by clarifying that "any measurable" daytime sleepiness is relevant to the assessment of the fitness to drive. In this meaning, but for reasons of general understanding, we here continue using the general term EDS.

Contrary to sleepiness (both in general and EDS), the concepts of "tiredness", "exhaustion" or even "fatigue", often originating from a very broad spectrum of psychogenic and chronic syndromes, are not very well accessible to latency measurements. Apparently, latency measures – especially MSLT-measurements – produce even paradox information: while physical activity improves (i.e. reduces) daytime sleepiness, the very broad and rather unspecific "tiredness" in the above mentioned syndromes is aggravated by physical activity, but cannot me measured in MSLT and MWT as these monotonous and soporific test situations do not represent a stimulus for sleep [35].

In consequence, the assessment of the fitness to drive in the case of a chronic medical condition relating to sleep critically hinges on evaluating daytime sleepiness (EDS) by way of MWT sleep-latency measurements. This is particularly important in order to assess treatment progress and/or treatment compliance.

Current guidelines provide orientation to assess the fitness to drive as based on MWT sleep latencies (**Table 3**). *Per definitionem* the MWT captures daytime sleepiness (EDS) at values <40 min. Empirical and normative data display that 97.5% of

Fitness to drive (lower categories)	Positive	Borderline positive	Borderline negative	Negative
MWT latency (average)	≥ 34 min	20–33 min		< 20 min
MWT latency (single)				< 20 min
single sleep fragments (<5 s)	normal	normal		
Multiple sleep fragments (<5 s)			X (repetition)	
Longer sleep fragments (>5 s)			X (repetition)	
Fitness to drive (higher categories)	**Positive**	**Borderline positive**	**Borderline negative**	**Negative**
MWT latency (average)	≥ 34 min			< 34 min
Any sleep fragements				X (6 month)

Table 3.
Evaluation of the fitness to drive based on MWT-sleep latencies and other parameters as measure in an MWT according to current guidelines [10].

healthy test subjects can stay awake for more than 8 min and 59% for 40 min or more [33, 36]. Current guidelines suggest a limiting MWT sleep latency of ≥34 min as the limit to a relevant "excessive daytime sleepiness" (EDS), corresponding well with the average sleep latency of 36.5 min [28]. However, the guidelines allow leeway in as far as single sleep fragments and micro-sleep episodes might be allowed, although their existence strongly recommends repeating the MWT after a reduced control interval and/or improved therapy.

4. Relevant conditions in traffic medicine

As has become clear in Section 2 of this chapter, traffic medicine is – in some way - a statutory service institution. Assessments are by order of (and paid for by) the driver but serve the issuing authorities in deciding if or under which conditions a driving license can be (re)-granted. The assessment covers all medical fields (see MMR). While unclear conditions or problems might prompt further inquiries to associated specialists, Traffic medicine is far from being a diagnostic or a treatment institution, but rather a "medical detective's office".

This position encompasses, that a broad knowledge, long-term experience and a keen eye/ear for potential inconsistencies in the stories told by drivers form the basis of – often very standard and uniform - daily assessments and control exams.

This includes also, that many of the more severe or chronic conditions are, in fact, managed by the family physician and associated specialists. Higher-level expert in traffic medicine might thus check and confirm a lower level assessment of a managing doctor based on records and statements, but might not see the patient directly. To give an example unrelated to this books topic, a well-controlled diabetic is only rarely required to undergo a level 4 exam. Similarly, well-documented state of treatment positive and compliant patients with affective disorders are sufficient.

The same applies to the large field of conditions affecting sleep: Severe conditions immediately prompt the action of specialists and might lead to immediate revocation of a driver's license, be it permanent or until successful treatment is documented according to guidelines. With respect to sleep conditions, it is rather

the unclear cases, *post hoc* assessments of accidents and substance/medication-related issues – mostly involving the danger of EDS – that are present in traffic medicine.

4.1 Conditions leading to EDS

It is evident from the preceding chapters, that the symptom of a measurable daytime-sleepiness (EDS) stemming from either behavioral aspects or medical conditions is most relevant to traffic medicine in the assessment of the fitness to drive. In the following section, we provide a brief overview over the prevalence and the different medical conditions associated with EDS.

For lack of a general public health definition of EDS accessible to large-scale public health studies, the determination of the prevalence of EDS has proven to be difficult. With estimated prevalence ranging between 3.2 to 32.5% as reported in [37], valuable information for orientation is provided by yearly polls of the U.S. National Sleep Foundation [38]. The 2008 poll reports, that around 30% of participants concede to sleepy/drowsy driving at least once per month during the last year, mostly to and from work ([39], p. 32). While this number is highly subjective, ESS-data provide a slightly less subjective or more systematic orientation about self-assessed sleepiness: accordingly, 18% of the participants scored 10 or more points qualifying them as excessively sleepy with increased likelihood of medical conditions [40]. A more stringent report [37] analyzed data from 5,962 face-to face interviews within the National Comorbidity Survey Replication (NCS-R), resulting in a prevalence of EDS of 23%. This study identified individuals with significant impairment/distress due to "excessive sleepiness (ExS.)" based on reported sleepiness in conjunction with an irrepressible need for sleep, difficulty waking up and/or prolonged nighttime sleep that was unrefreshing [37].

In **Table 4**, we summarized and categorized possible origins for EDS by (a) Sleep deprivation, i.e. too little sleep in general, be it behavioral or situational, (b) Reasons for fragmented sleep be it for environmental or medical reasons, (c) Primary CNS related hypersomnia, including narcolepsy, (d) "True" neurological conditions that might be associated directly or indirectly with altered sleep e.) Psychiatric conditions often accompanied directly or indirectly with altered sleep and, lastly, (recreational or illicit) substances/stimulants or medications that typically induce EDS and/or sleepiness. Due to its focus on the outcome sleepiness, rather the table might seem somewhat arbitrary. However, this categorization should not be confused with a classification of sleeping disorders *per se* as in, for example [42], or the new ICSD-3 [30–32].

We therefore added coloring, indicating items in different categories that are accessible to similar treatment/changes. Accordingly, basically all reasons for sleep deprivation, sleep fragmentation by environmental reasons and most substance induced reasons for sleepiness/EDS are accessible to behavioral/situational change (light blue) Obstructive sleep apnea syndrome and Obesity Hypoventilation Syndrome are accessible to device assisted treatment (CPAP, APAP, servo ventilation, gray).

While narcolepsy and epilepsy are often well manageable with relatively mild medication (light red), many primary CNS hypersomnia and neurological conditions, including RLS and PLMD are less accessible to treatment or require more complex care management (gray-blue). Similarly, the most other organic conditions require complex medication including symptomatic pain relief (yellow, see opiates). Lastly, care and medication psychiatric conditions requires specialized attention with respect to EDS and sleepiness, in particular in the context of the fitness to drive (light green).

(a) Sleep deprivation	(b) Fragmentation of sleep	(c) Primary CNS hypersominas	(d) Neurological conditions	(e) Other organic causes	(f) Psychiatric conditions	(g) Substance or medication induced
Behavioral pattern	Obstructive sleep apnea syndrome	Narcolepsy	Neurodegenerative disorders (Parkinson Alzheimer)	Congestive heart failure	Depression and other affective disorders	Alcohol
Sleep hygiene	Restless leg syndrome	Idiopathic hypersomnia	Multiple Sclerosis	Chronic renal failure	Anxiety disorders	Stimulant overdose/ withdrawal (Nicotine, caffeine)
Altered sleep phases	Periodic limb movement disorder	Parasomnias	Stroke	Liver failure	Psychotic disorders	Sleeping pills
Jet lag	Environmental disturbances (noise, light)	Cyclic or episodic hypersomnia	Epilepsy	Malineoplastic and malignancy syndromes	Post-traumatic stress disorders	Drug abuse (Cannabis, cocaine)
Shift work	Central sleep apnea syndrome	Menstrual-related sleep disorder	CNS tumors	Obesity hypoventilation syndrome		Opiates, Benzodiazepines, Barbiturates
Stress, voluntary sleep rejection		Kleine-Levin Syndrome				Anti-epileptics, Gamma-Hydroxy-Butyrate (Xyrem)
						Antidepressant, Neuroleptic

Table 4.
Common causes of and contributors to EDS/sleepiness (modified after [41]).

As the occurrence of EDS is trivial or at least likely in cases of hypersomnia or neurological disorders, respectively, specialist case management addresses this danger usually in a very efficient manner. Consequently, traffic medicine rarely receives unclear cases stemming from these conditions. Rather, traffic medicine is usually only required to assess and document the requirement for regular reports of lower level experts - in most cases the patient's physician - to the authorities.

EDS can be caused, on the one hand, by short- or long-term (miss-) behavior (i.e. "partying) or working conditions such as night or shift work [43]. On the other hand, it can stem from medical conditions, such as narcolepsy [44], hypersomnia [45], OSAS [46], RLS [47], or medication, such as anti-histaminica or antidepressants [48, 49]. In the clinical setting, two of the most commonly encountered causes leading to EDS are obstructive sleep apnea, restless leg syndrome and periodic limb movement disorder [41]. Other reports count non-apnea sleep disorders higher in risk, but for all injuries, not limited to driving [50]. At the same time, several reports [51] indicate, that also sleep medication- or sleep medication-withdrawal-induced psychomotor impairments/disorders, such as REM-sleep behavior disorder, RBD, might lead to parasomnias and, in consequence, EDS [42].

While our own records indicate only 114 out of 256,387 entries indicate a clear sleep accident (search term "Einschlafunfall") of various origins, we do find 750 and 1,904 entries for the term OSAS or sleep apnea (search term "Schlafapnoe"), respectively 170 entries are retrieved for sleeping problems (search term "Schlafstörung"), 125 for restless-leg syndrome and 111 entries for narcolepsy. Only 17 entries can be retrieved for hypersomnia.

The potentially multifactorial origin of EDS shows exemplarily the importance of a full anamnesis and complete medical examination in traffic medicine. We illustrate this by way of a case study.

4.2 Case study 1: uncovering a case of OSAS-induced EDS

One morning in March, around 7 am, a 62-year-old man drove at moderate speed on a straight street to work. According to eyewitnesses, the driver's car moved more and more towards the lane of the oncoming traffic. After two small grazing collisions, a frontal collision at moderate speed ended the drive. The driver reported a "blackout" and declared no recollection of the initial grazing collisions or ignition of the airbags. He reported to be "fully back" immediately after the frontal crash. He stepped out of the car unharmed, called the police helped the other driver and secured the site. Subsequently, a "wave-like" uneasiness with low pulse (40 bps) set in, which lasted for around 3 hours. As neither he nor the police could clearly identify a sleeping incident and he claimed a blackout, the police revoked his driving license based on a first-time TLoC until final assessment in traffic medicine. He was hospitalized for 3 days for both security and further check-ups.

For the traffic medical exam, which took place 5 months later in August, the patient presented himself in good physical and mental conditions. He reported to be in good health, to have been active, to drink usual amounts of alcohol and to be fully drug-naïve. He reported plans to retire abroad the following year after 40 years of successful work. He is unable to explain the blackout, as he has driven this route to work about "100,000 times".

Extensive medical exams included cardiological, neurological and neuro-angiological reports, including overnight EEG. While epileptiform spike-patters were observed when falling asleep, these were considered norm variants and not to causative for a blackout. However, strong snoring and a medium-grade OSAS was reported with an AHI of 33 although this was restricted to unusual sleeping positions (back). The patient was surprised about this finding and reported to notice no

negative physical effects of this condition. Only, his wife moved out of the bedroom due to the snoring. As there was no evidence excluding a TLoC and indication for an OSAS – although without clear signs of EDS – the permission to drive was not re-granted. This assessment could be reconsidered, provided the patient had proof for no further TLoC-like events within a year and could provide a repeated polysomnographic examination for confirmation of the moderate state of his OSAS.

The patient presented himself 13 months later (September) with the following records: A second PSG (performed December the previous year) reported a severe OSAS with AHI of 77, ESS 3/27 with subjectively normal sleep. At this point, a MWT was performed, but was considered non-evidentiary, such that there is no result reported. APAP treatment was initiated in January. An MWT performed in May confirmed inconspicuous (4 x > 40 min) with very good patient compliance. The snoring had subsided and the wife had moved back into the shared bedroom. Despite clear signs for a sleep accident, the initial round of examinations only revealed unclear results, except indications for an un-diagnosed sleep condition (OSAS) from the wife's reports and a first nighttime-EEG. Here the patient's compliance is exemplary. Based on this and no further indication of a TLoC-like event, the assessment supported re-granting the license on the condition of yearly follow-up reports. Most likely due to his retirement and relocation abroad the patient was lost to follow-up in our files.

In conclusion, it is in the interest of the individual driver's safety and traffic safety in general to obtain a full anamnesis and medical examination in traffic medicine. While traffic medicine is primarily neither a diagnostic nor therapeutic instance, traffic medicine's unique perspective, mandate and its concomitant in-depth assessment of the medical fitness to drive allows detecting previously unreported cases of EDS.

However, an EDS based on medical condition might be obscured or – vice versa - incorrectly assumed, when other conditions require medication that potentially leads to sleepiness. This will be highlighted in the following chapter that introduces the dimension of depression, age and behavior in the context of inappropriate use of medication, such as antidepressants and sleeping pills.

5. Substance (ab/mis)use and the fitness to drive

As outlined in Section 2, active participation in traffic requires adequate physical and psychological performance and reserve capacities. With any medication or substance taken, one's overall performance might improve or worsen. While many substances might reduce performance in a noticeable, but manageable fashion, some might induce (daytime) sleepiness. This is particularly true for most psychoactive substances, either in its wanted or unwanted effects (such as lag, hangover, rebound, side effects, and paradox reactions).

Somewhat trivial but not always known, this is clearly true for sleeping pills, (hypnotics/ hypnosedativa), but also for medication in psychiatric disorders (antidepressants, antipsychotics), allergies (antihistaminic) and, partially, degenerative disorders (e.g. Parkinson) [52]. Therefore, traffic medicine needs to know how to evaluate the fitness and the ability to drive under the influence of such medication. As described in the first paragraphs of this section, this is particularly important if such medication is combined, as often – but not exclusively - the case of elderly drivers.

We then provide a brief sketch of historic improvements and persisting problems of the above classes of drugs, with a focus on potential issues for safe driving

related to sleep, leading general recommendations for experts based on a classification by the International Council on Alcohol, Drugs and Traffic Safety, ICADTS. Subsequently we evaluate potential issues of excessive self-medication (melatonin, doxylamine) and the (ab)use of (illicit) drugs such as cannabis, barbiturates and opioids. By way of a case example, we highlight the value of hair sampling for controlling long-term substance (ab)use.

5.1 The triangle depression, sleep, and age

According to a recent report of the Swiss health observatory (Obsan) from 2016 [53], a substantial fraction of the Swiss population feels heavily (5%) or moderately to heavily (13%) burdened with mental and psychological problems. Consequently, 18 out of 100 are likely to present mental disorders. Yearly prevalence varies by year: most frequent are anxiety disorders (14%), affective disorders (7.8%), somatoform disorders (4.9%) and alcohol-related disorders (3.4%). Almost 90% of all affective disorders are depressions (6.9% of total). Around 5% of the Swiss population take either hypnotics on a daily basis. About 40% of the population with mental problems take antidepressants. In both groups, women are more prevalent, and the incidence increases strongly with age [54]. Importantly, there are indications that there is a gender difference in driving performance when using hypnotic medication [55].

While antidepressants alone might have strong effects on driving performance via sleep disturbance [14], initial symptom of above mentioned mental disorders (or of the prolonged stress periods leading to mental disorders), is heavily disturbed sleep, directly linking an increased use and prescription of psychopharmaca to that of hypnotic medication, i.e. sleeping pills, the latter often being benzodiazepines or Z-Drugs [53].

These figures have increased in the last decades [56] and steep increases in these figures are to be expected as a consequence of the severe social restriction due to the corona pandemic. Here, sleep patterns that are altered due to the lack of social control (school, home-office, retirement and lack of social contacts) might themselves contribute to the etiology of psychiatric disorders and stress-syndromes, in particular in children and adolescents. Conversely, the demographic increase of elderly drivers with increasing rates of comorbidities and concomitant multimedication might potentiate the relevance of drug interactions in traffic on the other side of the age spectrum. However, even without age-related conditions or depression, the elderly often report sleep issues, which are loosely remedied by standard hypnotics, such as Z-Drugs and benzodiazepines, or self-medication by off label use. [57]

Here, many patients naively presume that prescribed or OTC medication does not pose a risk in traffic and do not even mention taking it in an assessment. Similarly, the addictive potential of some of the medication and "doctor hopping" to obtain a desired drug should not be underestimated, even in highly regulated markets such as Switzerland. Such unmonitored self-medication might result in adverse side effects and unexpected drug interactions.

5.2 General recommendation for prescribing doctors and classification of medication

In any case, the above unknowns poses a series of problems for both prescribing doctors and experts in traffic medicine. Whenever assessing the FTD or prescribing new medication experts should answer the following set of questions:

- Does a medication have positive and/or negative effects on physical and mental performance and reserve capacity required for safe driving, and if yes, how much? Is the result balanced?

  In other words: Does the medications main effect sufficiently increase physical and mental performance and reserve capacity required for safe driving? Do the medication's undesired effects lower the physical and mental performance and reserve capacity required for safe driving?

- How long the medication should be prescribed?
- Are there long-term consequences of the treatment (Parkinson, L-Dopa, wear-off effects), indicating negative progression and thus narrower control intervals of the FTD?
- Is there addictive potential associated with the drug?
- Is the medication taken correctly? Are compliance and adherence given?
- Do any indications exist, that call for checking adherence/compliance by blood-level testing or similar?

While information relating medication to accident risks or odds ratios exists [57], it is limited and painstaking to collect. However, both on the acute level (i.e. the ability to drive) and the long term (the fitness to drive) it is widely undisputed that psychotropic drugs do affect the capabilities for safe driving: very simply speaking, hypnotic, sedatives and antidepressants are prescribed to calm down, to lower activity level and/or to fall asleep. It seems, on the one hand, thus, rather trivial that these desired effects might have spill-over-effects of the ability to drive.

It is not trivial on the other hand, to collect and categorize the existence and, subsequently, the extent of such effects on safe driving. Thankfully, the large-scale EU-Project DRUID (Driving Under the Influence of Drugs) that included participation of the ICADTS presented an aggregated list of medications affecting safe driving [58, 59] and published according prescription guidelines [57].

Listed drugs were classified as follows:

I. Presumed to be safe or unlikely to produce an effect

II. Likely to produce minor or moderate adverse effects

III. Likely to produce severe effects or presumed to be potentially dangerous

All antidepressants/-psychotics and hypnotics are listed in category II or III. The most relevant drugs are listed in **Table 5**, possibly a helpful tool for both physicians and experts.

Wherever know, detailed information is provided as to how long not to drive after changes in the respective medication. As a general rule of thumb from the perspective of traffic medicine, patients should abstain from driving for a period of about 14 days after treatment start, change or end of a treatment regime.

With every change in medication, the effects of prescribed drugs as well as the duration of effects on driving should be explained in detail. The recommendation to abstain from driving and the warning information should be registered in the

Active ingredient	Classification	Active ingredient	Classification
ANTIPSYCHOTICS		**BENZODIAZEPINES + Z-DRUGS**	
Levomepromazine	III	Diazepam	III
Fluphenazine	II	Chlordiazepoxide	III
Perphenazine	II	Oxazepam	III
Thioridazine	III	Potassium clorazepate	II
Haloperidol	II	Lorazepam	III
Melperone	II	Bromazepam	III
Pipamperone	II	Alprazolam	III
Benperidol	II	Flurazepam	III
Flupentixol	II	Nitrazepam	III
Zuclopentixol	II	Flunitrazepam	III
Clozapine	II	Triazolam	III
Olanzapine	II	Lormetazepam	III 1 mg (capsule): >10 hours post dosing little or no impairment (Category I)
Quetiapine	II	Temazepam	III 10 mg: >10 hours post dosing little or no impairment (Category I)
Sulpiride	II	Midazolam	III
Amisulpride	II	Zopiclon	III
Lithium	II	Zolpidem	II 10 mg: >10 hours post dosing little or no impairment (Category I)
Risperidone	II	Zaleplon	II 10 mg: >5 hours post dosing little or no impairment (Category I)
Clotiapine	II		
ANTI-DEPRESSANTS		**ANTI-DEPRESSANTS**	
Desipramine	II	Paroxetine	I
Imipramine	II	Sertraline	I
Clomipramine	II	Fluvoxamine	I
Trimipramine	III	Escitalopram	I
Amitriptyline	III	Moclobemide	I
Nortriptyline	II	Mianserin	III
Doxepin I	II	Trazodone	III
Melitracen	II	Mirtazapine	III
Fluoxetine	I	Venlafaxine	I
Citalopram	I		
		STIMULANTS	
		Dexamfetamine	II
		Methylphenidate	II

Table 5.
Classification of hypnotics, anti-depressants and -psychotics, stimulants with respect to effects on driving according to the DRUID study [58] in collaboration with ICADTS [60]. Excerpt from [59].

patient's records. After the initial treatment phase, patients should be controlled. If there are clinical sings of, for example generally lowered response time, reduced vigilance, reduced speed of perception processing or motoric effects, the patient should not be allowed to drive as these severely affect the reserve capacity for safe driving substantially.

In particular, drugs carrying an addictive potential should not be prescribed for long terms and their appropriate (therapeutic) dosage and use should be confirmed by blood-level testing.

5.3 Disappointed & false expectations: sleep medication and its effect on driving in a historical perspective

Disturbances of sleep have always troubled humanity [61]. Sleep medicine as a subject field in medicine has only evolved rather late (c. since the mid 1970s) but fulminant [62]. This especially after linking mayor breakthroughs in measurement technologies, findings and concepts such as the electroencephalogram, EEG [63], detection of sleep-stages [64] including rapid eye movement sleep, REM, [65], to the regulation and control of circadian rhythms and chronobiology [26, 66, 67].

Before bromides solutions emerged in the 1800s, it was mostly alcohol and drugs such as opium and cannabis that served to induce or facilitate falling asleep. The first effective synthetic hypnotic was chloral hydrate in 1869, followed by paraldehyde around 1880 and the introduction of the first of a long series of barbiturates (phenobarbital, 1912) after initial synthesis of the founding compound barbital in 1903.

While the above substances were introduced well before the public had widespread access to such medication or, for that matter, driving, their addictive potential and recreational use remain a problem in traffic medicine today.

Between the first and second world war, the extensive, indiscriminate and uncontrolled use of barbiturates (and for that matter other drugs [68]) such as, phenobarbital, secobarbital, amobarbital and pentobarbital in the general population coincides with an increase of cars and traffic density.

This increase in cars and traffic density accelerated drastically with the beginning of the second half of the 20th century, motivating a further evolution of traffic medicine, more and more including the control of addictive substances. This development parallels a boost in the development in sleep medicine (see above) but also coincides with the development and increasingly widespread use of the next generation of hypnotics, the benzodiazepines, which today are still one of the most widely prescribed group of medication.

The lower number of unfavorable side effects of benzodiazepines as compared to barbiturates led to brad use as a household hypnotic, severely underestimating the development of tolerances, addiction and side effects. As above mentioned for early sleep remedies, the (by-)use of benzodiazepines in recreational settings keeps this class of hypnotic well in the focus of traffic medicine even nowadays [14] .

Much like in other, earlier cases (radium, heroin, pervitin [68]) the repeated promise of "side-effect-free" medicine proved to be naïve and incorrect again. In particular, benzodiazepines are associated with a rather large number of psychomotor disorders indirectly affecting sleep in a negative way [51].

Initially, this seemed to be different with a new group of hypnotics, arriving in the late 1980ies: the non-benzodiazepines, often called Z-Drugs [69], promised to be specific and highly effective hypnotics. However, identical pharmacodynamics as compared to benzodiazepines indicate paths to similar side effects. These are, however, sometimes slightly less pronounced or just different: Z-Drugs seem to have lower tendency for physical dependence and addiction, but are known to

produce amnesia and, rarely, hallucinations. Counterintuitively, some of the Z-Drugs double the risk of developing depression and some long-terms studies found a marked increase in suicide risk [70]. Zolpidem itself is associated with rebound insomnia, possibly resulting in subsequently aggravated EDS. In Contrast to zolpidem and zopiclone, zalepon is not associated with an increased risk of motor vehicle accidents [71]. However, effects of Z-Drugs on human performance including some rather bizarre behavioral effects heavily affecting sleep have been summarized [69].

Nowadays, swift and thorough testing the effects of novel - and supposedly again more specific - hypnotics on driving performance [72] prevents major surprises in novel sleep medication with respect to effects on driving performance. This includes orexin system blockers, such as Suvorexant [73] and Lemborexant [74], or melatonin agonists [66, 67], such as Ramelteon [71, 75].

This also applies to reevaluation of older information [76, 77] concerning driving performance after the "rediscovery" of some tricyclical antidepressants, such as doxepin (Silenor) [78] which effectively trigger sleep onset in an antihistamine-like fashion, i.e. by selectively blocking H1-receptors.

As mentioned above for the older generations of dedicated hypnotics, older generations of other medication have been - and are still - used to facilitate or induce sleep based on their side effects. However, the negative consequences on driving performance might however be even more pronounced than in modern hypnotics. Depending on a countries medical system, this self-medication is more or less uncontrolled. Here in particular, ab- or miss-use of over the counter drugs might be risky in traffic. Additionally, some of these substances are likely to be part of an addictive behavior. Some substances have even become literally "traditional" to the degree of "folklore". To mention here directly are, among others, first-generation antihistamines such as doxylamine (e.g. Sanalepsi, Unisom), diphenhydramine (e.g. Benadryl, Nytol), but also partially available antitussives such as codeine (e.g. Mucatussin) but also the inappropriate use of melatonin pills with questionable results on sleep, but potentially sever impacts on driving performance [79–81].

With this plethora of information to deal with, it is to be expected that unintended and uniformed misuse of individual or combined medication might lead to sleepiness on the wheel, potentially resulting in severe accidents. Similar to unknown medical conditions, it is again traffic medicine's mandate to "elucidate" the exact or at least most likely cause of such accidents. Very often a thorough anamnesis and sighting of all available records is insufficient to give conclusive results. It is then, that modern tools of forensic pharmacology and toxicology come into play, much like in the case of drug checking [82]. Unless take at – or in timely context of – the incident urine and blood sampling suffer from the low diagnostic window and are mostly useless. In contrast, high-resolution hair-sampling might provide valuable information over considerable time-spans [83], which also allows to confirm or falsify previous information form anamnesis or testimonials.

5.4 Case study 2: uncovering a medication induced sleep accident

One morning in May, a fifty-year-old woman cased an accident on the highway in commuter traffic. She reported to have nodded off, causing the accident in consequence. She also stated to have taken the sleeping pill Zolpidem and the antidepressant Trazodone the evening before and an additional antidepressant (Sertraline).

The toxicological examination of blood revealed in fact Zolpidem and Trazodone in therapeutic concentrations and Sertraline in sub-therapeutic concentrations.

Accordingly, the toxicological assessment postulated an improper use of the hypnotic, as Zolpidem was detected at such high concentrations in the morning, despite its short half-life. According the ability to drive (ATD) at the time of the accident was impaired due to improper medication. Accordingly, the road safety authorities ordered for a full traffic medical assessment including a traffic medical examination at level 4.

Here, the women reported to have started taking Trazodone two years prior to the accident as she had developed sleeping problems due top psychosocial problems. Trazodone and Sertraline had been prescribed by her psychiatrist. Additionally, her practitioner had prescribed Zolpidem from time to time. She reported to have taken Zolpidem only rarely, as she had gotten to know of its addictive potential. At the time of the examination, she had ceased to take Zolpidem already for a period. She explained the situation and the resulting accident by accidentally mixing up Zolpidem and Sertraline.

A routine laboratory set for drugs was ordered, In addition, a segmented hair analysis was performed to confirm discontinuation of Zolpidem use.

Status: The patient presented herself in good general condition, cardiopulmonally compensated, no neurological defects, and psych status after MADP inconspicuous/nondescript.

Therapy at exam: Trazodone, Sertraline.

Routine Laboratory:

Urine: Tetrahydrocannabinol (THC), Cocaine, Methadone, Benzodiazepines, Amphetamine, Methamphetamine, Opiates, Barbiturates, Ecstasy, Buprenorphine, Zolpidem, Tramadol, Fentanyl, Ketamine, MDA, Methaqualone, Methylphenidate, Oxycodone, Phencyclidine, Propoxyphene, Spice/K2, Zaleplon: negative, **Trazodone, tricyclic anti-depressants: positive.**

Hair Analysis Results: (Benzodiazepins und Z-Drugs):

1. Segment: ca. 3 cm (proximal, younger, estimated July–September): Zolpidem 49 pg./mg

2. Segment: ca. 2 cm (distal, older, estimated April–June): Zolpidem 120 pg./mg

In all, anamnestic and laboratory information was sufficient to conclude, that there was no continued medication ab- or misused. The information supported the patient's explanation of a singular medication mistake. The patient was compliant and adherent. The MMR's are given and the fitness to drive could be affirmed.

6. Concluding summary

By way of data form so-called "developed" countries we illustrate a striking prevalence of and, subsequently, an imminent threat for traffic safety by sleep-related disorders. In line with the ambition to minimize fatalities, Switzerland approaches mitigating such (and other medical) threats by defining medical minimum requirements for a driving license. Regular or incidence-related control of these requirements in a highly structured process in traffic medicine reflects one possible strategy that is logically consistent with highly regulated health care, administration and society in general. However, the threat form sleepy driving is universal and fundamentally independent of "development" or location. Thus, consolidated expert advice depends largely on facilitated exchange of unequivocal information, potentially even at the danger of oversimplification. In this line, we argue for a more consistent use of the term "sleepiness" and its signs. We

furthermore suggest a more consistent use of standardized measurements (MWT) to detect excessive (or existent) daytime sleepiness (EDS) as the most relevant consequence of sleep conditions met most often in traffic medicine (OSAS, narcolepsy, substance induced EDS). It is often not strikingly bizarre sleep disorders but rather unidentified ones that present the highest risks for traffic. Thus, we inform about simple but clear signs of sleepiness. This is to sensitize both practitioners and experts. These should have an open eye a.) for the interplay between seemingly unrelated conditions potentially leading to EDS affecting the fitness to drive and b.) for the relevance of uncontrolled, uninformed and unintentional substance ab- and misuse affecting the ability to drive. In particular, the latter aspect depends not only on a particular legal and administrative framework's setup, but also on the general or individual attitude in society.

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Conflict of Interest

The authors declare to have no conflicts of interest.

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