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SERIES "THE GENETIC AND CARDIOVASCULAR ASPECTS OF OBSTRUCTIVE SLEEP APNOEA/HYPOPNOEA SYNDROME"
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Epidemiology of sleep apnoea/hypopnoea syndrome and sleep-disordered breathing

P. Jennum* and R.L. Riha#

ABSTRACT: Epidemiological studies have revealed a high prevalence of sleep-disordered breathing in the community (up to 20%). A subset of these patients has concurrent symptoms of excessive daytime sleepiness attributable to their nocturnal breathing disorder and is classified as having obstructive sleep apnoea/hypopnoea syndrome (4–5% of the middle-aged population). There is strong evidence for an association of sleep apnoea with cardiovascular and cerebrovascular morbidity, as well as adverse public health consequences. Treatment and diagnosis have remained largely unchanged over the past 25 yrs. In moderate-to-severe obstructive sleep apnoea/hypopnoea syndrome, treatment with continuous positive airway pressure has been shown to be effective. Questions remain as to how to screen patients with sleep-disordered breathing. Should time-consuming diagnostic procedures with high sensitivity and specificity be employed, or should simpler methods be applied for screening populations at risk, *e.g.* in the primary care sector?

KEYWORDS: Epidemiology, sleep apnoea, sleep-disordered breathing

The epidemiology of obstructive sleep apnoea (OSA)/hypopnoea syndrome (OSAHS) has been described in a significant number of studies. OSAHS affects ~2–4% of the middle-aged population and is defined on the basis of symptoms of daytime sleepiness and objective measures of disordered breathing during sleep. Obstruction of the upper airway during sleep, resulting in repetitive breathing pauses accompanied by oxygen desaturation and arousal from sleep, is characteristic of OSAHS. This results in diurnal sleepiness leading to cognitive impairment. Sleep-disordered breathing (SDB; snoring and associated apnoeas) is common and affects up to 20% of the population.

OSAHS is common in adults and children. OSAHS is an independent risk factor for hypertension and is associated with cardiovascular and cerebrovascular morbidity. OSAHS has consequences for public health (driving, accidents at work) and the economy. The benefits and effects of continuous positive airway pressure (CPAP) treatment have been described in prospective studies. Despite increasing awareness of the condition and improved diagnostic procedures, most patients in the community remain undiagnosed and untreated. This is especially true of patients who may be at high risk for additional complications, *e.g.* those with metabolic syndrome, diabetes, or cardiac, cerebrovascular or other neurological diseases. Few or no public health programmes have included systematic screening for OSAHS. Traditionally, OSAHS is diagnosed using in-hospital, supervised overnight polysomnography (PSG) followed by manual titration of CPAP. This is costly, both time-wise and economically, and since the capacity of this procedure is limited, waiting lists tend to lengthen. This calls for discussion of an organisational model not only for the identification and management, but also for the prevention, of OSAHS and its consequences. The present article focuses on the epidemiological aspects of OSAHS and SDB, risk associations, socioeconomic consequences and organisational aspects of diagnosing and managing sleep apnoea.

AFFILIATIONS
*Danish Centre for Sleep Medicine Glostrup, Denmark.
#Dept of Sleep Medicine Royal Infirmary of Edinburgh, Edinburgh, UK.

CORRESPONDENCE
P. Jennum
Danish Centre for Sleep Medicine,
Dept of Clinical Neurophysiology,
Faculty of Health Sciences
University of Copenhagen
Glostrup Hospital
DK 2600 Glostrup
Denmark
Fax: 45 43233933
E-mail: poje@glo.regionh.dk

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EPIDEMIOLOGY

Sleep apnoea has been recognised throughout human history, dating as far back as the 4th century BC. Numerous reports throughout the 19th century and the early part of the 20th century AD gave way to systematically conducted studies on patients with OSAHS and related syndromes [1].

OSAHS was first properly documented in neurophysiological sleep laboratories using techniques developed for the investigation of other conditions such as depression and narcolepsy. OSAHS was first described as such in 1965 [2] and there has since been an explosion in the facilities for its diagnosis and treatment as well as a rapid advancement in the understanding of its far-reaching consequences.

Reporting of OSAHS was initially confined to case series, but more recently, large-scale epidemiological studies have attempted to answer questions on the incidence and prevalence of OSAHS. However, few of these have used ideal methods and it is therefore difficult to draw firm conclusions from them.

Generally, the best-conducted studies, in terms of method and rigour of technique employed, have found a prevalence of OSAHS in the middle-aged male population of up to 4% [3]. The study showing the lowest quoted prevalence may have underestimated the occurrence of OSAHS in the population by using oximetry alone, with more than five 4% dips in pulse oximetry-measured arterial oxygen saturation per hour, as an initial screening measure [4], while those studies showing the highest prevalences may have overestimated the prevalence by including central apnoeas and breath-holds occurring during wakefulness [5] using inductance plethysmography at home. Assessment of sleepiness differed between the studies on account of using self-devised questionnaires specific to each study. Fewer studies exist examining the prevalence of OSAHS in females but it is probably half that of males, at 0.5–1% [5].

OSAHS occurs throughout the entire lifespan, from neonates to the elderly. In adults, the frequency of disordered breathing during sleep increases with age and is poorly associated with an increased incidence of daytime sleepiness or other symptoms of OSAHS [6–10].

ASSESSMENT OF OSAHS

As discussed above, a definitive diagnosis of OSAHS requires objective recording and measurement of sleep and breathing during the night in addition to a measure of daytime sleepiness (objective or subjective) and other symptoms.

SDB

An objective measure of SDB at night is generally required to confirm the diagnosis of OSAHS. The method most widely used, and which is considered by some to be the ''gold standard'' for diagnosis despite limited evidence, is overnight PSG. An American Academy of Sleep Medicine (AASM) Task Force published indications for PSG in 1997 [11] and measurement techniques and syndrome definitions in 1999 [12]. Most PSG studies monitor the following routinely: nasal and/or oral airflow; thoracoabdominal movement; snoring; electroencephalogram (EEG); electro-oculogram; electromyogram; and oxygen saturation. Signal collection and interpretation is usually computerised, but manual scoring of the trace should still be performed using guidelines for interpretation of the EEG published in 1968 by RECHTSCHAFFEN and KALES [13], and the 1999 AASM criteria [12].

Full-night PSG is generally performed, but split-night studies are also used [14], in which the first half of the study night is used for diagnosis and the second half to monitor treatment response using CPAP.

Cardiorespiratory monitoring alone can also be used. This involves the measurement of airflow, respiratory effort, oxygen saturation and cardiac frequency, but not EEG. The great advantages of these systems are price, portability and the ability of patients to monitor themselves at home. FERBER *et al.* [15] reviewed seven studies of portable ambulatory monitoring systems and reported a sensitivity of 78–100% and a specificity of 67–100% in comparison with in-lab PSG, although ambulatory monitoring is of course not a gold standard.

Overnight oximetry is sometimes used as a screening test for identifying patients who are at risk of significant OSAHS, but this should never be seen as a substitute for in-lab PSG or home cardiorespiratory monitoring. There are severe limitations inherent in this technique used in isolation, including the inability to detect apnoeas or hypopnoeas not associated with oxygen desaturation and the upper airway resistance syndrome. Furthermore, nocturnal oxygen desaturation may be related to sleep hypoventilation without associated upper airways obstruction, *e.g.* in chronic obstructive pulmonary disease (COPD), severe kyphoscoliosis, muscular dystrophy and morbid obesity, and in the setting of periodic breathing associated with severe heart failure.

Daytime sleepiness

Sleepiness is difficult to define (see [16] for a review). Sleepiness can be regarded as ''normal'' sleepiness (a result of the normal circadian rhythm) and ''pathological'' sleepiness (a result of altered sleep scheduling). Pathological sleepiness can be further subdivided into ''habitual'' (*e.g.* as the result of recurring precipitants of sleepiness such as OSA) or ''occasional'' (*e.g.* as the result of jet lag or medication).

As proposed by CLUYDTS *et al.* [16], sleepiness can be recognised using a number of different measures. 1) Inferring sleepiness from behaviour, *e.g.* observation of yawning frequency, actigraphy, facial expression or performance tests such as the driving simulator, psychomotor vigilance tests and reaction time tests. 2) Self-evaluation of sleepiness using rating scales, *e.g.* the Stanford Sleepiness Scale to measure sleepiness at a given instant, and the Epworth Sleepiness Score (ESS) to measure sleepiness averaged over a month. 3) Direct electrophysiological measures, *e.g.* multiple sleep latency test and multiple wakefulness test [17], pupillometry and cerebral evoked potentials.

In respect to the diagnosis and monitoring of OSAHS, probably the most widely used and best-validated scale assessing daytime sleepiness is the ESS, first devised in 1991 [18]. Its advantages include ease of administration and low cost. It assesses global level of sleepiness and is independent of short-term variations in sleepiness with the time of day and also of inter-day variations [19]. The ESS aims to measure the general level of daytime sleepiness as a stable individual

characteristic and has satisfactory test–retest reliability [20]. The ESS is also able to discriminate between normal and pathological sleepiness [20]. The accuracy of the ESS depends on the awareness of subjects falling asleep, which may not always be the case [21]. Rating of the subject's sleepiness by another person may be more precise [22]. The ESS does not correlate strongly with more objective measures of daytime sleepiness such as the multiple sleep latency test (MSLT) or maintenance of wakefulness test (MWT) [23], but this is in keeping with the fact that sleepiness is not a unitary concept. ESS reproducibly reflects changes in sleepiness with therapy in OSAHS [24]. Because of its reliability and its ability to differentiate between abnormal and normal levels of sleepiness, as well as for its ease of administration, the ESS is one of the most widely used measures of sleepiness.

In summary, self-reporting of snoring, nocturnal gasping or apnoeas and measures of sleepiness (*e.g.* ESS) correspond relatively poorly with objective measures, such as sound recording, apnoea/hypopnoea index (AHI) and MSLTs/MWTs [25]. Any relationship between these factors depends on the standardisation and the value of the reference test/gold standard and is subject to high variability in the validity of questionnaire and test evaluation. Complaints of sleepiness and/or other indications of hypersomnia are related to many other conditions, not just SDB, which weakens the relationship further.

Epidemiological studies have used a variety of methods to measure OSA, including self-reported markers such as snoring, apnoeas, daytime sleepiness, in-laboratory PSG, unattended in-home PSG, and unattended polygraphic or other recordings of a few physiological parameters. Studies using objective measures of apnoea and hypopnoea have employed variable respiratory event definitions. Moreover, there has been no standardisation of the method used to quantify airflow, with methods such as thermistry, inductance plethysmography and nasal cannula/pressure transducer systems providing different sensitivities to changes in airflow. Like other conditions based on a severity continuum, the definition of the units of the continuum and the ultimate thresholds used to designate the presence of OSA will affect the magnitude of prevalence and estimates of associations with risk factors and outcomes. The use of more-restrictive definitions of apnoea and hypopnoea, higher AHI cut-off points, or an additional requirement for symptoms of sleepiness, will obviously lower prevalence estimates and affect values expressing associations, such as odds ratios. Like other conditions, OSAHS presents a severity spectrum which affects the estimates of prevalences. Studies have consistently found that symptomatic OSAHS occurs in $\geqslant$2–4% of the adult population. Studies evaluating the occurrence of SDB, independently of symptoms, show a much higher prevalence of 6–24% among adults (tables 1–3).

SEX AND AGE

OSAHS is more common in males than in females, with a ratio of 2:1. Menopause is a risk factor for sleep apnoea [26]. OSAHS prevalence increases in mid-life, but the existence of OSAHS in childhood, adolescence and older age means that there is no simple positive correlation of OSAHS with age [27]. A multimodal distribution of prevalence by age is often indicative of distinct disease subtypes with different aetiologies and health consequences. SDB occurs commonly in populations aged >65 yrs (tables 1–3), but there is controversy regarding its significance in older people and its relationship to OSAHS that occurs in middle age [28, 29].

RISK ASSOCIATIONS

Smoking

Smoking is one of the strongest risk factors for cardiovascular disease. The association with OSAHS is relatively weak, but smoking may interact with and add to the cardiovascular risk associated with OSA [30].

Genetics/family history

Reports published in the 1990s suggested a relationship between self-reported snoring and familial occurrence of snoring and sleep apnoea, with a relative risk association of 3–5 [31–33]. The risk has been demonstrated to increase if both parents are affected. A number of studies have documented this association. A recent review of this evidence has evaluated this relationship [34]. In addressing this topic, future studies should address the hereditary components of OSAHS by subdividing the disease according to different subgroups, *e.g.* sleep apnoea with age of onset of disease, hypertension, metabolic syndrome, propensity to cerebrovascular disease and other risk associations.

TABLE 1 Age- and sex-specific prevalence rates of the apnoea/hypopnoea index (AHI) based on polysomnographic (PSG) results for a sample of 1,050 males and 1,098 females from the Vitoria-Gasteiz region of Spain

Age yrs	AHI				
	$\geqslant$5	$\geqslant$10	$\geqslant$15	$\geqslant$20	$\geqslant$30
Males					
30–39	9.0 (2–16)	7.6 (0–15)	2.7 (1–5)	2.1 (0–4)	2.1 (0–4)
40–49	25.6 (14–37)	18.2 (9–27)	15.5 (7–24)	10.1 (5–15)	7.0 (3–11)
50–59	27.9 (17–38)	24.1 (15–34)	19.4 (11–27)	14.7 (8–21)	11.4(6–17)
60–70	52.1 (33–71)	32.2 (17–48)	24.2 (12–37)	15.0 (8–22)	8.6 (4–14)
Females					
30–39	3.4 (0–7)	1.7 (0–4)	0.9 (0–2)		
40–49	14.5 (3–25)	9.7 (0–19)			
50–59	35.0 (20–50)	16.2 (5–27)	8.6 (1–17)	8.3 (0–16)	4.3 (0–10)
60–70	46.9 (31–63)	25.6 (13–38)	15.9 (6–26)	13.0 (3–22)	5.9 (0–13)

Data are presented as % (95% confidence interval). Data were collected as follows. The MESAM IV portable recording system (Medizintechnik für Artz und Patient, Munich, Germany) was used overnight. PSG was recorded using Alice 3 (Respironics, Pittsburgh, PA, USA). Manual scoring using conventional criteria was employed. An abnormal breathing event was defined as complete cessation of airflow for $\geqslant$10 s (apnoea) or a discernible 50% reduction in respiratory airflow accompanied by a decrease of $\geqslant$4% in arterial oxygen saturation measured by pulse oximetry and/or electroencephalogram arousal (hypopnoea). Arousals were defined according to American Sleep Disorders Association criteria [15]. Reproduced from [6], with permission from the publisher.

TABLE 2 Age- and sex-specific prevalence rates of the apnoea/hypopnoea index (AHI) based on polysomnographic (PSG) results for a sample of 352 males and 250 females from Wisconsin, USA

Age yrs	AHI		
	⩾5	⩾10	⩾15
Males			
30–39	17.0 (9.6–25)	12.0 (5.4–19)	6.2 (1.9–10)
40–49	25.0 (18–32)	18.0 (11–24)	11.0 (6.7–16)
50–60	31.0 (21–40)	14.0 (7.5–20)	9.1 (5.1–13)
Females			
30–39	6.5 (1.4–11)	4.9 (0.6–9.8)	4.4 (1.1–7.3)
40–49	8.7 (4.2–13)	4.9 (1.7–8.1)	3.7 (1.0–6.5)
50–60	16.0 (5.2–26)	5.9 (0.0–12.0)	4.0 (0.0–10)

Data are presented as % (95% confidence interval). Data were collected as follows. Overnight in-lab PSG recording was carried out in sound-attenuated, light- and temperature-controlled rooms using standard set-up and a 16-channel polygraph (Model 78d; Grass Instrument, Quincy, MA, USA). Manual scoring using conventional criteria was employed. An abnormal breathing event was defined as complete cessation of airflow for ⩾10 s (apnoea) or a discernible 50% reduction in respiratory airflow accompanied by a decrease of ⩾4% in arterial oxygen saturation measured by pulse oximetry. Reproduced from [3], with permission from the publisher.

TABLE 3 Prevalence rates of the apnoea and hypopnoea index (AHI) by age based on polysomnographic (PSG) results for a sample of 741 males from two counties in Southern Pennsylvania, USA

Age yrs	Subjects	AHI		
		⩾5	⩾10	⩾20
20–44	236	7.9 (5.0–12.1)	3.2 (1.6–6.4)	1.7 (0.6–4.4)
45–64	430	19.7 (16.2–23.7)	11.8 (9.1–15.3)	23.9 (15.7–34.9)
65–100	75	30.5 (21.1–41.7)	23.9 (15.7–34.9)	13.3 (7.3–23)

Data are presented as n or % (95% confidence interval). Data were collected as follows. Overnight in-lab PSG recording was carried out in sound-attenuated, light- and temperature-controlled rooms using standard set-up and a 16-channel polygraph (Model 78d; Grass Instrument, Quincy, MA, USA). Manual scoring using conventional criteria was employed. An abnormal breathing event was defined as complete cessation of airflow for ⩾10 s (apnoea) or a discernible 50% reduction in respiratory airflow accompanied by a decrease of ⩾4% in arterial oxygen saturation measured by pulse oximetry. Reproduced from [7], with permission from the publisher.

Obesity and metabolic syndrome

There is strong epidemiological and clinical evidence for a relationship between sleep apnoea, central obesity and metabolic syndrome. Despite the lack of controlled studies, several studies have presented data showing that weight reduction through dieting or bariatric surgery is followed by a reduction in AHI and incidence of diabetes, improved glucose control and reductions in hyper-triglyceridaemia [35–37]. This important area will be discussed further in the last paper in the current series.

Polycystic ovary syndrome

There is some evidence that sleep apnoea is associated with polycystic ovary syndrome [38, 39]; however, no epidemiological, cross-sectional or prospective studies have addressed this important issue.

CONSEQUENCES OF OSA

Morbidity and mortality associated with OSAHS

Untreated OSAHS can contribute to the development or progression of other disorders. OSAHS has now been shown to be a cause for systemic hypertension [40] and there is some evidence suggesting that it can also cause pulmonary hypertension [41, 42]. OSAHS is also associated with ischaemic heart disease.

SDB has been found to be a significant clinical feature in a proportion of patients with cerebrovascular disease: stroke and transient ischaemic attacks [40]. However, published results are contradictory, with some showing no increase in OSAHS in those with transient ischaemic attacks [43], while others show a high prevalence of OSAHS in those with stroke (see [44] for review).

Treating OSAHS in stroke is also controversial. Some studies show a significant reduction in SDB and improvement in quality of life, while others do not [45, 46]. Patients with OSAHS and moderate-to-severe coexistent lung disease, such as COPD, are more likely to develop type II respiratory failure that will improve with treatment of the obstructive apnoeas [47, 48]. Likewise, nocturnal asthma may be worsened by sleep apnoea and treatment may lead to improvement [49].

OSAHS leads to neuropsychological impairment that includes deficits in attention, concentration, vigilance, manual dexterity, visuomotor skills, memory, verbal fluency and executive function [50]. Perhaps the most important complication of OSAHS, and the one that has the greatest impact from the public health perspective, is driving accidents. More than one-third of patients with OSAHS report having had an accident or near-accident on account of falling asleep while driving [51]. There is also objective evidence of 1.3–12-fold increases in accident rates among those with sleep apnoea, and accident rates in OSAHS patients have been found to be 1.3 to seven times higher than those in the general population [52–54]. Vigilance testing and driving simulators in studies assessing driving performance in patients with OSAHS reveal that performance is markedly reduced and the impairment is not limited to periods when patients actually fall asleep but also occurs when they are awake, owing to reduced vigilance. There is also evidence that OSAHS patients have a 50% increased risk of workplace accidents [55, 56].

OSAHS thus leads to several complications, including: impairment in education, quality of life and work capacity; traffic accidents; cardiac and cerebrovascular morbidity and mortality; and increased economic burden.

Hypertension

A relationship between sleep apnoea, snoring and hypertension was proposed in the first half of the 1980s. This relationship was

initially supported by epidemiological studies using self-reported snoring as a surrogate marker for sleep apnoea [55, 57]. Later follow-up studies suggested that sleep apnoea was correlated with increased cardiovascular risk [58]. Although snoring is associated with hypertension, several studies questioned the link, taking other risk factors into consideration [59]. This is due to the problem with self-reported snoring: it shows only a partial relationship to sleep apnoea, with moderate sensitivity and specificity. Since then, several studies have shown a relationship between sleep apnoea, apnoea severity and the occurrence of hypertension, independently of risk factors, such as age and obesity [40].

Cardiac disease

Over the past 25 yrs, several studies have documented snoring and OSAHS as risk factors for cardiac disease (artherosclerotic, acute myocardial infarction, arrhythmias). Morbidity and mortality risk is increased in the context of SDB, even when taking other risk factors into consideration [40].

Sleep apnoea and stroke

Based on cross-sectional epidemiological studies primarily using self-reported snoring, a relationship between snoring and stroke was proposed in the mid-1980s. Prospective studies have supported this relationship. The drawback of these studies, however, was the inaccuracy of the report of snoring due to the sensitivity, specificity and the individuality of this symptom, which weakens a potential relationship between sleep apnoea and stroke. Case–control studies suggest a potential relationship based upon historical report of sleep apnoea and PSG findings in stroke patients compared with control groups [60, 61]. There are, however, several issues in these patients, especially patients with stroke and sleep-related breathing problems. These include selection problems and stroke-induced SDB (*e.g.* pseudo-bulbar OSA, central apnoea and hypoventilation) which may add to the occurrences of sleep-related breathing disorders [62].

Traffic accidents

Noncommercial drivers with sleep apnoea are at a statistically significant increased risk of having a motor vehicle crash. Magnitude of daytime sleepiness and the severity of SDB were correlated with crash risk, while full treatment of sleep apnoea improves driver performance [63]. Untreated OSAHS increases societal costs due to traffic accidents and their consequences [64–66].

Socioeconomic consequences

The social and cardiovascular consequences of OSAHS seem most pronounced among patients of low socioeconomic status. This was found to be the case in a clinic population [67], but in a discharge register study from Sweden, socioeconomic status had a minor effect on the likelihood of hospitalisation and it was suggested that other factors, *e.g.* smoking and obesity, may influence this observed relationship [68]. It should be noted, however, that there is a tendency towards lower screening and diagnostic activity among people of lower social status.

OSAHS presents a significant socioeconomic burden due to comorbidity, healthcare utilisation in the primary and secondary healthcare sectors, use of medication, effects on employment and lost income. Treatment of OSAHS causes reduced morbidity, mortality and hospitalisation rates and this has been demonstrated to be cost effective [69–73].

SCREENING AND MANAGEMENT OF SLEEP APNOEA

Undiagnosed OSAHS is likely to be highly prevalent, even in countries where diagnostic facilities have been available for a long time. A significant proportion of the potential for improved diagnosis is in the primary care sector, and in high-risk groups, *e.g.* patients with acute and chronic cardiovascular or cerebrovascular disease, or diabetics. There is a need to evaluate the optimal organisational model for patient identification and management. Few studies have presented the optimal economic model for the evaluation of OSAHS. In a Danish Health Technology Assessment, the use of ambulatory portable diagnostic procedures using partial polygraphy followed by auto-adjusted CPAP was superior to the use of in-hospital, supervised PSG (which is time consuming and costly) and oximetry (which has low sensitivity and diagnostic accuracy) among patients without major comorbidity in the primary care sector [74]. Similar results have been obtained by others, who found oximetry to present low diagnostic accuracy, but also pointed out the use of split-night PSG studies as an alternative diagnostic and therapeutic approach [75]. Thus, there is a need to evaluate the organisation of diagnosing and managing patients with OSAHS, with and without major comorbidities. In patients without major comorbidity suspected of OSAHS, a portable study approach is possible [76], whereas in patients with significant neurological, cardiac or pulmonary disease it is likely that a supervised study is desirable [77].

CONCLUSION

In conclusion, it is impossible, in view of the vast quantity of literature that has burgeoned in the field of obstructive sleep apnoea/hypopnoea syndrome, to present an exhaustive overview of all its aspects. However, the following main messages remain: obstructive sleep apnoea/hypopnoea syndrome and sleep-disordered breathing are very common, affecting a significant proportion of the population and, when untreated, cause significant increased social, cardiac and cerebrovascular morbidity and mortality; a significant proportion of patients with obstructive sleep apnoea/hypopnoea syndrome remain undiagnosed and untreated due to inadequate resources for case detection and investigation. There is a need to identify optimal organisational and economic models to identify patients at risk for additional screening and management, especially in ''at-risk'' populations.

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