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References: 1. O'Byrne PM et al. N Engl J Med 2018; 378: 1865-76. **2.** Bateman ED et al. N Engl J Med 2018; 378: 1877-87. **3.** Beasley R et al. N Engl J Med 2019; DOI: 10.1056/NEJMoa1901963. **4.** Hardy J et al. Lancet 2019; Published online Aug 23, 2019; http://dx.doi.org/10.1016/S0140-6736(19)31948-8. **5.** Kuna P et al. Int J Clin Pract 2007 (May); 61(5): 725 – 36. **6.** Bousquet J et al. Respir Med 2007; 101: 2437 – 46. **7.** Sobieraj DM et al. JAMA 2018; doi: 10.1001/jama.2018.2769. **8.** Symbicort Hong Kong Package Insert. Feb 2021.

Presentation: Budesonide/Formoterol Turbuhaler. **Indications:** In adults and adolescents (12 years and older), for the treatment of asthma, to achieve overall asthma control, including the relief of symptoms and the reduction of the risk of exacerbations. Symptomatic treatment of moderate to severe COPD in adults. **Dosage:** **Asthma** ***1) Symbicort anti-inflammatory reliever therapy (patients with mild disease) 160/4.5 mcg Turbuhaler*** *Adult & Adolescent ≥ 12yr:* 1 inhalations as needed in response to symptoms. If symptoms persist after a few minutes, 1 additional inhalation should be taken. No more than 6 inhalations should be taken on any single occasion. A total daily dose of more than 8 inhalations is normally not needed, however a total daily dose of up to 12 inhalations can be used temporarily. ***2) Symbicort maintenance and reliever therapy*** *Adult & Adolescent ≥ 12yr:* Patients should take 1 inhalation of Symbicort Turbuhaler 160/4.5 mcg as needed in response to symptoms to control asthma. If symptoms persist after a few minutes, 1 additional inhalation should be taken. No more than 6 inhalations should be taken on any single occasion. Recommend maintenance dose is 1 inhalation b.d. and some may need 2 inhalations b.d.. A total daily dose of more than 8 inhalations is normally not needed, however a total daily dose of up to 12 inhalations can be used temporarily. ***3) Symbicort maintenance therapy 160/4.5 mcg Turbuhaler*** *Adult & Adolescent ≥ 12yr:* 1-2 inhalations b.d.. Max daily dose is 4 inhalations. **COPD** ***160/4.5 mcg Turbuhaler*** *Adult:* 2 inhalations b.d.. Max daily dose is 4 inhalations. **Contraindications:** Hypersensitivity to budesonide, formoterol or lactose. **Precautions:** Should be used for the shortest duration of time required to achieve control of asthma symptoms. Should only be used long-term in patients whose asthma cannot be adequately controlled on asthma controller medications. Not be used to initiate treatment with inhaled steroids in patients being transferred from oral steroids. It is recommended that the maintenance dose be tapered when long-term treatment is discontinued. Potential systemic effects of ICS, HPA axis suppression and adrenal insufficiency, bone density, growth, visual disturbance, infections/tuberculosis, sensitivity to sympathomimetic amines, cardiovascular disorders, hypokalaemia, diabetes, pneumonia, lactose, pregnancy & lactation. Not recommended for children below 12 years of age. Incidence of candidiasis can be minimized by having patients rinse their mouth out with water after inhaling their maintenance dose. **Interactions:** CYP3A4 inhibitors, beta-receptor blocking agents, other sympathomimetic agents, Xanthine derivatives, mineralocorticosteroids and diuretics, Monoamine oxidase inhibitors, tricyclic antidepressants, quinidine, disopyramide, procainamide, phenothiazines and antihistamines. **Undesirable effects:** Palpitations, Candida infections in the oropharynx, headache, tremor, mild irritation in the throat, coughing, hoarseness. **Full local prescribing information is available upon request.** API.HK.SYM.0721

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Editorial

There are three excellent articles in the issue, including an overview of the complicated simple snoring, a territory-wide study on e-cigarettes in Hong Kong, and a study on the importance of asthma written action plan in southern Taiwan.

The first article reviews the topic of complicated simple snoring. Primary snoring (PS) has historically been considered as a benign entity, however, increased evidence revealed its correlation to consequent cardiovascular and neurocognitive outcomes. Dr. Cheng provides an excellent review of PS including the definition, risk factors for progression, impact on cardiovascular and neurocognitive/behavioral systems, proposed mechanism, and treatment. PS is a common sleep disorder in children and it deserves more studies to illustrate its health implications and find the appropriate intervention to prevent consequent morbidities.

E-cigarette use is an emerging health issue of extreme concern in recent. In Hong Kong, it was worrying that adolescents accounted for 37.4% of e-cigarette users and were the most popular age group. The second article reported a study on e-cigarettes. Dr. Yeung surveyed 26,684 secondary-school students on sociodemographic characteristics, self-reported harms of e-cigarette use, and their relationship with smoking intention, habits, and quitting intention. The study concluded that e-cigarettes were related to poor perceived health status and respiratory symptoms. E-cigarette use was also associated with the intention to use cigarettes and with no significant changes in quitting intention.

The third article investigated the importance of parental knowledge regarding components of written asthma action plans (WAAP) in asthma control in children in southern Taiwan. The use of a WAAP has been shown to improve lung function and reduce school absences, activity limitations, and emergency department visits. However, patients and parents sometimes receive WAAP and sometimes receive health education information about asthma directly. Ms. Wang and Dr. Huang *et al*. conducted a questionnaire-based survey on this issue and found that the asthma symptom control level was significantly and positively related to the understanding of key WAAP components. They expected that developing an easy-to-use WAAP and using it as a standard tool for asthmatic children would greatly improve asthma control in Taiwan.

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There are no conflicts of interest.

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Review Article

The Complicated Simple Snoring

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Abstract

Primary snoring, also known as simple snoring, was historically regarded as a benign entity on the sleep-disordered breathing spectrum until recently, when more and more evidence suggested the otherwise. This article aims to provide an overview on the research directions of primary snoring and their relevant clinical significance.

Keywords: Cognition, hypertension, obstructive sleep apnoea, primary snoring

A Continuum of Snoring?

Primary snoring (PS), also known as simple or non-apneic snoring, is a relatively common condition characterized by habitual snoring (HS) >3 nights per week and normal conventional polysomnography (PSG). Current estimation reported that 7.2% and 4.8% of children in Hong Kong suffered from HS and obstructive sleep apnoea (OSA) respectively.[1,2] Positioned at the milder end of sleep-disordered breathing (SDB) spectrum,[3,4] PS was historically regarded as a benign entity without causing significant medical consequences for the snorer and co-snorer until recently. As accumulating evidence has identified PS as an independent risk factor for complications described originally for OSA, such as poorer neurocognitive-behavioral function[5] and higher cardiovascular risks,[6] an urgent need for a paradigm shift in the current clinical thinking and management strategy of PS is hence required.

Definition of PS

Despite the high prevalence in the general population, currently, we see a lack of consensus regarding the cut-off and occasional requirements of PS. The distinction between PS and other sleep disorders is, conceptually and originally, based on the absence of clinical consequences. Previously, the 2005 American Academy of Sleep Medicine (AASM) International Classification of Sleep Disorders (ICSD-2) was amongst the most commonly cited definition of PS.[7] It defined PS as loud upper airway breathing sounds in sleep without episodes of apnoea or hypoventilation.[8] In 2014, the update by ICSD-3 recognized that an absolute absence of apnoea is not essential to delineate the difference in clinical outcomes of PS and other sleep disorders.[9] Since then, <1 apnoea/hypopnoea events per hour of sleep on the Apnoea-Hypopnoea Index (AHI) in the absence of any clinical consequences was commonly used to identify PS in research settings.[7] It is also worth noticing that this working definition is arbitrary, without reliable clinical validation, and varies between studies.

Meanwhile, it is clear that AHI alone may not be sufficient to define PS. In 2016, Kryger redefined PS based on the duration, oxygen saturation, airflow limitation, and the level of anatomical obstruction in the hopes to model the absence of any physical implications due to PS.[10] For the psychological aspect, i.e., to study the disturbance to patients and possibly the co-sleepers, a noise approach that looks into sound patterns and cut-offs of specific acoustic parameters may be appropriate.[11] The limitation of such an approach, however, lies in the subjectivity of individuals' perception of snoring, making objective

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quantification of nuisance from PS extremely difficult. Considering the dyadic nature of sleep, recent studies, such as the one by Genlyd *et al.* on noise exposure, promote the assessment of 'noise annoyance level' that include aspects such as 'daytime sleepiness' and 'tiredness' in the paired comparison.[12]

Currently, to distinguish PS from other sleep disorders, overnight PSG is the only currently available definitive investigation.[5] Diagnosis is made based on clinical history, the number of respiratory events per hour of sleep on PSG, and the corresponding physiological consequences in terms of gas exchange abnormalities and arousals. Some authors choose a composite respiratory disturbance score to diagnose PS based on several factors such as the extent of SpO2 desaturation and respiratory arousals.[13,14]

Risk Factors of HS and PS Progression

To the best of our knowledge, no studies have evaluated the risk factors of PS thus far. Studies reporting risk factors for HS may provide clues for the predictor of PS development. A large cohort across the Asia Pacific showed a higher prevalence of HS in males and Caucasians,[1] most probably due to their genetically determined craniofacial structure. Nonetheless, prematurely born children may be at a higher risk for snoring and SDB as well.[1] Additionally, the severity can be made significantly lower by breastfeeding for at least 2 months according to one study.[15]

Studies examining the natural history of PS are also scarce. Whether PS is associated with the development of other more severe sleep disorders, for example, OSA remains unclear. In a community-based follow-up study by Li *et al*, persistent snoring and overweight or obesity were found to be the risk factors for PS progression.[16] Persistent snoring, with its relatively high negative predictive value,[16] can hence be used as a guide for SDB progression. Meanwhile, weight reduction may play an important role in the management of PS. In addition, puberty has no significant effect on PS progression,[16] suggesting that changes in sex hormones were not a primary modulator of upper airway function during puberty. Neither sex nor adenotonsillar hypertrophy was identified as a significant predictor.[16]

Cardiovascular Impacts of PS

Emerging evidence has shown that childhood PS has adverse effects on the cardiovascular system,[17] rendering the need to identify and treat as soon as possible.

A local cross-sectional study by Li *et al.* published in 2009 was among the very few who first provided evidence on the potential cardiovascular risks in PS children.[18] By demonstrating that PS was an aspect of the dose-response relationship between SDB and blood pressure (BP), it provided a new insight contrary to the universal belief that PS was entirely benign. Nighttime BP particularly was found to be significantly higher in the PS cohort after adjusting for age, sex, and body mass index (BMI). The findings carry prominent significance in the sense that elevated childhood BP is associated with increased carotid intima-media thickness (cIMT) and arterial thickness, which are the preceding markers of atherosclerosis.[19] With a similar elevation in BP level during childhood, it predicts a worse prognosis of future cardiovascular adverse events, adult hypertension, and metabolic syndrome.[20]

The association between PS and endothelial function was first proposed by the same author in 2011, which showed a significantly reduced flow-mediated vasodilation (FMD) among PS children independent of body size and OAHI.[21] Unlike OSA, the mechanism underlying PS and impaired endothelial function is not associated with hypoxia, oxidative stress, and frequent arousals, as reflected by the insignificant differences in all respiratory parameters, arousal indexes, and sleep architecture between PS and controls in the same study. These results, inspiringly, provided grounds on the possibility that PS may not simply be a milder form of OSA, but a part of a more complex phenotype that is yet to be determined.

The causal association between childhood PS and undesirable cardiovascular outcomes is further supported by a recent longitudinal study by Au *et al.*[22] Predictive markers of cardiovascular disease (CVD), namely reduced FMD, increased cIMT, and elevated BP remained significant at 5-year follow-up of PS subjects aged 6 to 18 irrespective to the change of OSA severity. Strategies to alleviate upper airway narrowing and the resultant CVD burden should, therefore, not be overlooked. Though a proven treatment for childhood snoring is not currently available besides nasal steroids,[23,24] the study highlighted the clinical importance of regular monitoring for children with PS on their SDB and cardiovascular status.

Neurocognitive and Behavioral Impacts of PS

There is growing evidence that children with PS exhibit cognitive and behavioral deficits equivalent to children with OSA when compared to non-snoring controls.[25,26]

In a pioneer study by Blunden *et al.* published in 2000, a significant difference in cognitive functioning was accidentally found between snoring children and controls.[27] The unexpected finding sparked much intrigue surrounding the morbidity of PS. Subsequently, cognitive outcomes, such as IQ score, memory, attention, executive function, organization ability, motor coordination, verbal ability, and fluency, were investigated by various studies.[25,28-30] The observation of deficit in PS children is not universal. It is noted that in the majority of studies, results of cognitive assessment in PS subjects, even if found to be significantly lower than controls, still fall

within normative limits. This highlights that whether snoring is associated with cognitive impairment later in life still requires further investigation. However, the adverse effect of PS on cognitive functioning is still undeniable if we compare the percentage of PS children labelled with impaired cognition and those who are carefully matched to control.[31]

Studies have consistently shown behavioral impairment in children with PS.[13,27] Most commonly reported deficits include hyperactivity, inattention, and somatic complaints. A surprising finding was found in the Jackman *et al.* study in which the PS group exhibited the greatest deficit in a majority of the behavioral domains, followed by the mild OSA group.[32] Another cross-sectional study by Brockman *et al.* also reported that children with PS had a higher risk of inattentive behavior than those with OSA.[33] A 10-fold increase in sleepiness was observed as well in PS children compared to a 5-fold increase in the OSA group.[33] All evidence seems to be hinting that PS may not simply be a milder form of OSA at the SDB spectrum.

Proposed Mechanistic Pathways

Currently, the clinical outcomes of OSA are explained by the hypoxic insult to the developing brain and sleep disruption due to repeated arousals.[34] There has been an endeavor to evaluate if those physiological stresses also account for the deficit in PS. However, current data cannot depict the association.[31] It is possible that the subtle differences in oxygen level and sleep parameters could be missed using the conventional protocol. Measures of cerebral oxygenation in response to a respiratory event may be inaccurately reflected at the periphery and that excessive daytime sleepiness may not be a fit measurement for arousals. More objective assessments, such as differences in cerebral blood flow velocity[35] and sleep latency test,[36] may hence be required for further investigation.

Some of the neurocognitive and cardiovascular impacts of PS, nonetheless, can be explained by a large community-based study by Zhu *et al.* in 2014 consisting of 619 subjects.[37] Compared to non-snoring children, the percentage of slow-wave sleep (SWS) decreased significantly in the prepubertal PS group. SWS is associated with better neurocognitive functioning.[38] Meanwhile, the percentage of non-rapid eye movement stage 1 (N1) sleep as well as wake after sleep onset (WASO), a representation of sleep deficiency, were both significantly elevated in the pubertal sub-group. With less N1 sleep, impacted learning and memory are explained. Along with a study by Zhang *et al.* which showed the direct correlation between lower sleep efficiency (i.e. higher WASO) and increased sympathetic activity as reflected by a higher 24-hour urinary catecholamine level,[39] the critical role of PS in mediating cardiovascular complications is also conjointly manifested.

Treatment of PS

PS management can be conservative or non-conservative, depending on the associated underlying conditions. For snorers with obesity and orofacial myofunctional disorders (OMDs), for instance, weight loss and myofunctional therapy would be the first-line treatment respectively.[40] The AASM also recommends oral appliance (OA) therapy for PS in general.[41] There is currently no consensus on the optimal design of OAs but the therapeutic outcome in term of AHI and oxygen desaturation index (ODI) appear to be better if the device is custom-made.[42] It is worth noted that OAs, though effective, are associated with low compliance.[43] Meanwhile, surgical approaches like uvulopalatopharyngoplasty (UPPP) and adenotonsillectomy, though radical, are also available for patients with associated obstructed upper airway due to craniofacial anomalies as well as adenotonsillar hypertrophy. Till date, there are no drugs available for treating the primary pathology of PS.[44]

Conclusion

PS is a relatively common sleep disorder amongst the paediatric population. Although the original definition aims to delineate PS from OSA based on the absence of clinical consequences, increasing evidence revealed that snoring, even without associated changes in respiratory markers, may be associated with extensive cardiovascular and neurocognitive outcomes. More studies are required to elucidate the effects of PS on various disease development and appropriate action may be required to prevent these adverse outcomes.

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Conflicts of interest

There are no conflicts of interest.

References

1. Li AM, Sadeh A, Au CT, Goh DY, Mindell JA. Prevalence of habitual snoring and its correlates in young children across the Asia pacific. J Paediatr Child Health 2013;49:E153-9.
2. Li AM, So HK, Au CT, Ho C, Lau J, Ng SK, *et al*. Epidemiology of obstructive sleep apnoea syndrome in Chinese children: A two-phase community study. Thorax 2010;65:991-7.
3. Marcus CL. Sleep-disordered breathing in children. Am J Respir Crit Care Med 2001;164:16-30.
4. Anstead M, Phillips B. The spectrum of sleep-disordered breathing. Respir Care Clin N Am 1999;5:363-77, viii.
5. Marcus CL, Brooks LJ, Draper KA, Gozal D, Halbower AC, Jones J, *et al*.; American Academy of Pediatrics. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 2012;130:e714-55.
6. Horne RSC. Childhood snoring has long-term adverse effects on cardiovascular health. Respirology 2021;26:725-6.
7. De Meyer MMD, Jacquet W, Vanderveken OM, Marks LAM. Systematic review of the different aspects of primary snoring. Sleep Med Rev 2019;45:88-94.

8. Medicine AAoS. International classification of sleep disorders. Diagnostic and coding manual 2005:51-5.
9. Sateia MJ. International classification of sleep disorders-third edition: Highlights and modifications. Chest 2014;146:1387-94.
10. Kryger MH. Sleep and Breathing Disorders. E-Book. Elsevier Health Science; 2016. pp. 126-39.
11. Michael H, Andreas S, Thomas B, Beatrice H, Werner H, Holger K. Analysed snoring sounds correlate to obstructive sleep disordered breathing. European Archives of Oto-Rhino-Laryngology 2008;265:105-13.
12. Peterson TH. The "Genlyd" Noise Annoyance Model. Delta Report, 2007.
13. O'Brien LM, Mervis CB, Holbrook CR, Bruner JL, Klaus CJ, Rutherford J, *et al*. Neurobehavioral implications of habitual snoring in children. Pediatrics 2004;114:44-9.
14. Honaker SM, Gozal D, Bennett J, Capdevila OS, Spruyt K. Sleep-disordered breathing and verbal skills in school-aged community children. Dev Neuropsychol 2009;34:588-600.
15. Montgomery-Downs HE, Crabtree VM, Sans Capdevila O, Gozal D. Infant-feeding methods and childhood sleep-disordered breathing. Pediatrics 2007;120:1030-5.
16. Li AM, Zhu Y, Au CT, Lee DLY, Ho C, Wing YK. Natural history of primary snoring in school-aged children: A 4-year follow-up study. Chest 2013;143:729-35.
17. Deary V, Ellis JG, Wilson JA, Coulter C, Barclay NL. Simple snoring: Not quite so simple after all? Sleep Med Rev 2014;18:453-62.
18. Li AM, Au CT, Ho C, Fok TF, Wing YK. Blood pressure is elevated in children with primary snoring. J Pediatr 2009;155:362-8.e1.
19. Li S, Chen W, Srinivasan SR, Bond MG, Tang R, Urbina EM, *et al*. Childhood cardiovascular risk factors and carotid vascular changes in adulthood: The Bogalusa heart study. JAMA 2003;290:2271-6.
20. Verdecchia P, Schillaci G, Borgioni C, Ciucci A, Battistelli M, Bartoccini C, *et al*. Adverse prognostic significance of concentric remodeling of the left ventricle in hypertensive patients with normal left ventricular mass. J Am Coll Cardiol 1995;25:871-8.
21. Li AM, Au CT, Chook P, Lam HS, Wing YK. Reduced flow-mediated vasodilation of brachial artery in children with primary snoring. Int J Cardiol 2013;167:2092-6.
22. Au CT, Chan KC, Chook P, Wing YK, Li AM. Cardiovascular risks of children with primary snoring: A 5-year follow-up study. Respirology 2021;26:796-803.
23. Vlahandonis A, Walter LM, Horne RS. Does treatment of Sdb in children improve cardiovascular outcome? Sleep Med Rev 2013;17:75-85.
24. Leung TN, Cheng JW, Chan AK. Paediatrics: How to manage obstructive sleep apnoea syndrome. DIC 2021;10:1-14.
25. Bourke R, Anderson V, Yang JS, Jackman AR, Killedar A, Nixon GM, *et al*. Cognitive and academic functions are impaired in children with all severities of sleep-disordered breathing. Sleep Med 2011;12:489-96.
26. Miano S, Paolino MC, Urbano A, Parisi P, Massolo AC, Castaldo R, *et al*. Neurocognitive assessment and sleep analysis in children with sleep-disordered breathing. Clin Neurophysiol 2011;122:311-9.
27. Blunden S, Lushington K, Kennedy D, Martin J, Dawson D. Behavior and neurocognitive performance in children aged 5–10 years who snore compared to controls. J Clin Exp Neuropsyc 2000;22:554-68.
28. Beebe DW, Wells CT, Jeffries J, Chini B, Kalra M, Amin R. Neuropsychological effects of pediatric obstructive sleep apnea. J Int Neuropsychol Soc 2004;10:962-75.
29. O'Brien L, Mervis C, Holbrook C, Bruner J, Klaus C, Rutherford J, *et al*. Neurobehavioral implications of habitual snoring in children. Pediatrics 2004;114:44-9 .
30. Beebe DW, Ris MD, Kramer ME, Long E, Amin R. The association between sleep disordered breathing, academic grades, and cognitive and behavioral functioning among overweight subjects during middle to late childhood. Sleep 2010;33:1447-56.
31. Biggs SN, Nixon GM, Horne RS. The conundrum of primary snoring in children: What are we missing in regards to cognitive and behavioural morbidity? Sleep Med Rev 2014;18:463-75.
32. Jackman AR, Biggs SN, Walter LM, Embuldeniya US, Davey MJ, Nixon GM, *et al*. Sleep-disordered breathing in preschool children is associated with behavioral, but not cognitive, impairments. Sleep Med 2012;13:621-31.
33. Brockmann PE, Urschitz MS, Schlaud M, Poets CF. Primary snoring in school children: Prevalence and neurocognitive impairments. Sleep Breath 2012;16:23-9.
34. Halbower AC, Mahone EM. Neuropsychological morbidity linked to childhood sleep-disordered breathing. Sleep Med Rev 2006;10:97-107.
35. Hill CM, Hogan AM, Onugha N, Harrison D, Cooper S, McGrigor VJ, *et al*. Increased cerebral blood flow velocity in children with mild sleep-disordered breathing: A possible association with abnormal neuropsychological function. Pediatrics 2006;118:e1100-8.
36. Gozal D, Wang M, Pope DW Jr. Objective sleepiness measures in pediatric obstructive sleep apnea. Pediatrics 2001;108:693-7.
37. Zhu Y, Au CT, Lam HS, Chan CC, Ho C, Wing YK, *et al*. Sleep architecture in school-aged children with primary snoring. Sleep Med 2014;15:303-8.
38. Kaemingk KL, Pasvogel AE, Goodwin JL, Mulvaney SA, Martinez F, Enright PL, *et al*. Learning in children and sleep disordered breathing: Findings of the tucson children's assessment of sleep apnea (tucasa) prospective cohort study. J Int Neuropsychol Soc 2003;9:1016-26.
39. Zhang J, Ma RC, Kong AP, So WY, Li AM, Lam SP, *et al*. Relationship of sleep quantity and quality with 24-hour urinary catecholamines and salivary awakening cortisol in healthy middle-aged adults. Sleep 2011;34:225-33.
40. Camacho M, Guilleminault C, Wei JM, Song SA, Noller MW, Reckley LK, *et al*. Oropharyngeal and tongue exercises (myofunctional therapy) for snoring: A systematic review and meta-analysis. Eur Arch Otorhinolaryngol 2018;275:849-55.
41. Ramar K, Dort L, Katz S, Lettieri C, Harrod C, Thomas S, *et al*. Clinical practice guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: An update for 2015. J Clin Sleep Med 2015;11:773-827.
42. Ilea A, Timuș D, Höpken J, Andrei V, Băbțan AM, Petrescu NB, *et al*. Oral appliance therapy in obstructive sleep apnea and snoring - systematic review and new directions of development. Cranio 2021;39:472-83.
43. De Meyer MMD, Vanderveken OM, De Weerdt S, Marks LAM, Cárcamo BA, Chavez AM, *et al*. Use of mandibular advancement devices for the treatment of primary snoring with or without obstructive sleep apnea (Osa): A systematic review. Sleep Med Rev 2021;56:101407.
44. Achuthan S, Medhi B. A systematic review of the pharmacological approaches against snoring: Can we count on the chickens that have hatched? Sleep Breath 2015;19:1035-42.

Original Article

E-Cigarettes: An Emerging Threat to the Respiratory Health of Our Next Generation

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Abstract

Introduction: Given dramatic rises in electronic cigarette (e-cigarette) use among adolescents and ongoing dilemmas regarding their harms versus potential for harm reduction, this study examined the current pattern of e-cigarette use, the perceived health effects of e-cigarettes and the association of e-cigarette with the use of other tobacco products among Hong Kong secondary school students. **Materials and Methods:** 26,684 Hong Kong secondary school students participated in the territory-wide, school-based Hong Kong Secondary School Smoking and Health Survey 2016/17, conducted by the HKU School of Public Health. Data regarding demographics, self-reported harms of e-cigarette use, and its association with smoking intention, habits and quitting intention, was obtained and analysed. **Results:** Among Hong Kong secondary school students, 8.9% have ever-used e-cigarettes and the prevalence of past-30-day e-cigarette use was 3.0%. For those who had ever used e-cigarettes, 27.1% had their first puff before or at 11 years old. E-cigarette use among secondary school students was significantly associated with chronic respiratory symptoms (current users: AOR 1.59, 95% CI 1.13–2.23; ever users: AOR 1.36, 95% CI 1.22–1.53) and poorer perceived health status (current users: AOR 1.57, 95% CI 1.08–2.27; ever users: AOR 1.33, 95% CI 1.14–1.56), after adjusting for confounders. Current adolescent e-cigarette use was also significantly associated with increased intentions of tobacco smoking (AOR 1.17, 95% CI 1.12–2.46) and waterpipe use (AOR 2.63, 95% CI 1.77–3.91) in the next 12 months, cigarette smoking status (including those who ever-smoked, experimented, quit and currently smoke), and waterpipe and other tobacco product use in the past 30 days. Moreover, Hong Kong secondary school students who used e-cigarettes along with cigarettes did not show significant changes in quitting intention. **Conclusions:** E-cigarette use was associated with poorer perceived health status and respiratory symptoms, increased use and intention to use cigarettes and other tobacco products, and no significant changes in quitting intention. This study does not support e-cigarettes as a harm reduction tool and shows that e-cigarettes are not safe as general consumer products. Their function as a gateway to smoking and their failure to reduce quitting intention in adolescents may renormalize the tobacco industry and reverse all tobacco control efforts.

Keywords: E-cigarettes, electronic cigarettes, gateway, respiratory health, smoking cessation

Introduction

Tobacco is the top preventable cause of respiratory morbidity and mortality worldwide. Whilst Hong Kong's tobacco smoking rates has been on the decline over the past few decades, ranking amongst the lowest in the world at 10.0%,[1] a new potential threat to respiratory health of our next generation has emerged.

Electronic cigarettes (e-cigarettes) are devices that facilitate nicotine intake through a vaporized 'e-liquids', consisting of varying levels of nicotine, flavorings and additives, without tobacco combustion.[2] Global e-cigarettes usage surged from 7 to 35 million within 5 years between 2011–2016, and is projected to rise even further to 55 million by 2021.[3] In 2017, the Tobacco Control Policy-related Survey by the Hong Kong Council on Smoking and Health (COSH) showed that 3.5% of respondents have ever used e-cigarettes. Yet, it was alarming to note that 37.4% of e-cigarette users

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were adolescents aged 15–29, which was drastically more than any other age group.[4]

The rapidly growing youth and adolescent e-cigarette user-base, bolstered by successful youth-directed marketing with diverse e-cigarette packaging and flavor choices,[5] is especially concerning. In 2016/17, the prevalence of e-cigarette use among secondary and primary students were 8.7% and 1.4% respectively.[6] In particular, a local study revealed that the percentage of Primary 2 to 4 pupils who had tried e-cigarettes increased by 55% within a year from 2016/17 to 2017/18.[7] Given that substance use is typically established during early adolescence, it is important to develop a greater understanding on the impact of e-cigarette usage amongst youths due to its implications on their short-term and long-term health.

However, there have been fervent debates over whether e-cigarettes are in fact harm-reducing or harm-inducing. E-cigarettes have been marketed as healthier alternatives for cigarettes that could also aid smoking cessation. On the other hand, numerous public health experts around the world have been calling for a ban on e-cigarettes, citing mounting evidence of its negative health impact and potential as a gateway to nicotine addiction and youth smoking.[8] Hence, this study was conducted among Hong Kong secondary school students with the following objectives:

1) To assess the current pattern of e-cigarette use among HK secondary school students
2) To analyze the perceived health effects of e-cigarettes among Hong Kong secondary school students
3) To evaluate the association of e-cigarette with the use of other tobacco products among Hong Kong adolescents

Materials and Methods

A territory-wide, school-based survey on smoking among Secondary 1 to 6 students was conducted by the HKU School of Public Health in 2016–17. Data regarding demographics, self-reported harms of e-cigarette use, and its association with smoking intention, habits and quitting intention, was obtained. SPSS Statistics 25 was used for analysis. Sociodemographic characteristics and e-cigarette smoking behaviour were summarized using descriptive statistics. Chi-squared tests were used to compare factors associated with e-cigarette use, intention of use, health effects and associations with other tobacco products. Adjusted odds ratios (AOR) were calculated using logistic regression, adjusting for age, sex, place of birth, perceived family affluence, parental education, housing type, and, where appropriate, cigarette smoking status or use of other tobacco products in the past 30 days.

Results

Pattern of e-cigarette use

A total of 26,684 secondary school students participated in the survey. Baseline characteristics are described in [Table 1].

Table 1: Baseline characteristics of 26,684 sampled subjects

n = 26,684	n	% (SD)	*n* = 26,684	n	% (SD)
Age (Mean±SD)		14.8 ± 1.74	Housing type		
<11 years old	84	0.3%	Public	12055	45.5%
12 years old	2533	9.5%	Subsidized	1090	4.1%
13 years old	4256	16.0%	Private	9664	36.5%
14 years old	4834	18.1%	Temporary/ Others	1925	7.3%
15 years old	4910	18.4%	Do not know	1772	6.7%
16 years old	5470	20.5%	Perceived family affluence		
17 years old	3089	11.6%	Relatively poor	1825	6.9%
18 years old	1034	3.9%	Poor to average	6475	24.4%
19 years old	297	1.1%	Average	14898	56.0%
>20 years old	141	0.5%	Average to rich	2872	10.8%
Gender			Relatively rich	510	1.9%
Boy	14575	54.7%	Father's education		
Girl	12073	45.3%	Primary or below	2861	10.8%
Place of Birth			Secondary	12948	48.7%
Hong Kong	20073	75.4%	Post-secondary	4579	17.2%
Mainland China	5619	21.1%	Do not know	6213	23.4%
Macau	228	0.9%	Mother's education		
Taiwan	108	0.4%	Primary or below	3366	12.7%
Other places	579	2.2%	Secondary	13525	50.9%
			Post-secondary	4057	15.3%
			Do not know	5641	21.2%

Among Hong Kong secondary school students, 8.9% have ever-used e-cigarettes and the prevalence of past-30-day e-cigarette use was 3.0%. For those who had ever used e-cigarettes, 30.4% had smoked in the past 30 days and 5.3% were frequent users (i.e. used e-cigarettes for more than 20 days in the past 30 days). 27.1% had their first puff before or at 11 years old (primary school age), and 86.9% before 16 years old [Table 2].

The major reasons cited for using e-cigarettes were 'easy to use at home unnoticed' (19.8%), 'curiosity' (17.2%), 'like the flavours' (10.6%), 'attractive and trendy' (7.9%), and 'less harmful to health' (4.1%). 48.1% of e-cigarette users did not know whether their e-cigarettes contained nicotine. 24.5% never, 15.7% occasionally and 11.7% always used nicotine-containing e-cigarettes. Fruits were the most popular flavour among youth (43.4%), followed by mint (19.0%) and candy (12.2%). Only 3.1% smoked e-cigarettes with no flavour [Table 3].

Among those who did not use e-cigarettes, 9.8% were susceptible to use (i.e. did not have strong determination

Table 2: E-cigarette smoking status and age of initiation

	n	%		n	%
E-cigarette use			Age of smoking the first electronic cigarette puff		
Never used	24191	**91.1%**	<7	39	5.0%
Ever used	2366	**8.9%**	8	28	3.6%
Have quit now	2121	**8.0%**	9	37	4.7%
Used once/few times	1464	5.5%	10	44	5.6%
Prev. occasionally use, quit now	493	1.9%	11	65	8.3%
Prev. use every day, quit now	164	0.6%	12	93	11.8%
Current use	245	**0.9%**	13	131	16.6%
Occasionally use	121	0.5%	14	145	18.4%
Use every day	124	0.5%	15	102	13.0%
			16	103	13.1%
Number of days of e-cigarette use in the past 30 days			Intention to use e-cigarettes in next 12 months		
0 day	25781	97.0%	Definitely not	23992	90.2%
1–2 days	272	1.0%	Probably not	1564	5.9%
3–5 days	187	0.7%	Probably will	770	2.9%
6–9 days	120	0.5%	Definitely will	261	1.0%
10–19 days	83	0.3%			
20–29 days	33	0.1%			
30 days	98	0.4%			

Table 3: Reasons for using e-cigarettes

	n	%		n	%
Reasons for using e-cigarettes			Nicotine-containing e-cigarettes		
Seems easy to use at home unnoticed	533	19.8%	None	190	24.5%
Curiosity	462	17.2%	Some	122	15.7%
Like the flavours	285	10.6%	All	91	11.7%
Friends also use	250	9.3%	Do not know	374	48.1%
Attractive and Trendy	211	7.9%	Flavours of e-cigarettes		
Seems less harmful to health	110	4.1%	Fruits	519	43.4%
Other reasons	105	3.9%	Mint	227	19.0%
Relieve boredom	93	3.5%	Candy	146	12.2%
Gift from friends	81	3.0%	Coffee	115	9.6%
Relieve stress	77	2.9%	Tobacco	61	5.1%
Family also use	75	2.8%	Alcohol	59	4.9%
Easier to be bought	69	2.6%	No Flavour	37	3.1%
Cheaper	68	2.5%	Spice	33	2.8%
Want to quit smoking	61	2.3%	Others	93	7.8%
Want to reduce smoking	56	2.1%			
Seems generate less SHS	56	2.1%			
Seems easy to use at school unnoticed	51	1.9%			
Seems able to use anywhere	43	1.6%			

Table 4: Association of sociodemographic factors with e-cigarette use and intention of use

Socio-demographics	Intention to use in next 12 months		
	No	Yes	AOR (95% CI)
	%	%	
Age			1.21 (1.17–1.25)*
Male sex (vs. female)	54.0%	59.1%	1.21 (1.09–1.35)*
Born in HK (vs. abroad)	76.0%	71.2%	1.03 (0.90–1.18)
Perceived family affluence (vs. average or above)			
Below average	3.2%	5.2%	1.67 (1.25–2.23)*
Parental education level at secondary or below (vs. tertiary or above)			
Father's education secondary or below	63.3%	58.4%	1.05 (0.94–1.17)
Mother's education secondary or below	19.5%	16.6%	1.08 (0.92–1.26)
Housing			
Private (ref. group)	34.9%	28.9%	1.00
Public/Subsidized	57.5%	62.2%	1.30 (1.15–1.48)*
Temporary/Other	7.6%	8.9%	1.301 (1.05–1.61)*

to not use e-cigarettes), and 3.9% had intentions to use e-cigarettes in the next 12 months [Table 2]. Sociodemographic factors associated with a greater intention to use e-cigarettes among non-users in the next 12 months were older age, male sex, below-average perceived family affluence, living in public/subsidized housing [Table 4]. The intention to use e-cigarettes also significantly increased with increasing number of peers using e-cigarettes, especially perceiving that 5 or more peers use e-cigarettes, as well as e-cigarette use in any family member, including father, mother, siblings, other relatives or maids (all $P < 0.001$) [Table 5]. Those who perceived e-cigarettes more positively and believed that e-cigarettes were not harmful were also significantly more likely to have intentions of using e-cigarettes. The most commonly cited favourably perceptions that were associated with increased intentions to use were 'better acceptance' (AOR 6.032, 95% CI 4.525–8.039), 'attractive and trendy' (AOR 3.72, 95% CI 3.04–4.55) and 'having fewer harms' (AOR 3.51, 95% CI 2.89–4.28) [Table 6].

Health effects of e-cigarette use

[Table 7] shows the association of e-cigarette usage with respiratory symptoms. Among secondary school students, 29.3% of ever e-cigarette users and 34.4% of current users reported having respiratory symptoms, such as cough or sputum, for over 3 months in the past year, as compared to 23.2% among all students. E-cigarette use was significantly associated with having chronic respiratory symptoms, including ever-users (AOR, 1.36; 95% CI, 1.22–1.53), experimenters, and current users (AOR 1.59, 95% CI 1.13–2.23).

As for self-perceived health status, 24.8% of e-cigarette ever-users and 39.3% current users reporting fair to poor health (versus good to excellent), as compared to 15.1% among all secondary school students. Poorer perceived health status was significantly associated with ever use (AOR, 1.33; 95% CI, 1.14–1.56) and current use of e-cigarettes (AOR, 1.57; 95% CI, 1.08–2.27). Significant associations were also observed in e-cigarette experimenters, ex-smokers and current daily users [Table 8].

Passive e-cigarette smoke exposure has also been shown to have significant health effects. Increased number of days of passive e-cigarette smoke exposure at home over the past 7 days was significantly associated with fair to poor perceived health status. Likewise, increased number of days of passive e-cigarette smoke exposure outside home over the past 7 days was significantly associated with fair to poor perceived health status and respiratory symptoms, as compared to good or excellent [Table 9].

The health effects of e-cigarettes were also compared to traditional cigarettes. E-cigarettes are generally perceived as less harmful and viewed more positively than cigarettes (both p-values<0.001) [Table 10]. While the percentage of cigarette smokers who had poorer perceived health status (38.3%) and respiratory symptoms (39.2%) were indeed higher than e-cigarette smokers (27.4% for perceived health status and 31.2% respiratory symptoms), no significant differences were observed between current cigarette and e-cigarette smokers' perceived health status (AOR, 1.49; 95% CI, 0.90–2.46) and respiratory symptoms (1.59, 0.97–2.62) [Table 11].

Association between e-cigarettes and other tobacco products

The association between e-cigarette, cigarettes and other tobacco products is explored in [Table 12]. For those who had never used e-cigarettes, the majority (92.5%) never smoked cigarettes, while 5.5% experimented, 1.3%

Table 5: Peer and Family Influence on Intention to Use E-cigarettes

Peer Influence	%	%	p-value from χ^2 test	AOR (95% CI)
Peer e-cigarette use			.000*	2.555 (2.417–2.701)*
None	87.3%	48.0%		1.000
1 - 2	9.3%	24.5%		4.405 (3.844–5.048)*
3 - 5	2.3%	15.0%		11.507 (9.645–13.729)*
6 - 10	0.5%	5.5%		22.039 (16.39–29.635)*
>11	0.6%	7.0%		22.317 (17.136–29.064)*
Perceived number of e-cigarette users in 100 peers			.000*	1.315 (1.281–1.350)*
0	8.9%	4.2%		1.000
1 - 4	14.0%	7.1%		1.214 (0.846 -1.743)
5 - 9	14.9%	9.1%		1.657 (1.177 -2.334)*
10 - 14	16.1%	12.0%		1.745 (1.245–2.446)*
15 - 19	14.9%	14.2%		2.405 (1.726 -3.352)*
20 - 29	13.7%	15.7%		2.945 (2.118 -4.095)*
30 - 49	10.2%	18.4%		5.017 (3.623 -6.947)*
50 - 69	3.4%	8.4%		7.095 (4.966–10.136)*
>70	3.8%	11.0%		8.172 (5.784 -11.546)*
Family Influence			p-value from χ^2 test	AOR (95% CI)
Father			.000*	
No	98.0%	96.1%		
Yes	2.0%	3.9%		1.951 (1.458–2.610)*
Mother			.000*	
No	99.3%	97.9%		
Yes	0.7%	2.1%		2.382 (1.505–3.770)*
Siblings			.000*	
No	99.3%	94.7%		
Yes	0.7%	5.3%		7.143 (5.337–9.561)*
Other relatives/maid			.000*	
No	99.0%	97.3%		
Yes	1.0%	2.7%		2.725 (1.898–3.913)*
Other people				
No	99.2%	97.2%		
Yes	0.8%	2.8%		4.293 (2.965–6.216)*
None			.000*	
No	5.3%	16.0%		
Yes	94.7%	84.0%		0.327 (0.278–0.384)*

quit and 0.7% were current smokers. Yet among current e-cigarette users, the majority (61.0%) concurrently smoked cigarettes, as compared to 20.7% who had quit, 10.4% who experimented and 7.9% who had never smoked cigarettes. Moreover, among current e-cigarette users, 38.4% used cigarettes, 19.2% used waterpipes and 59.6% used other tobacco products in the past 30 days.

Current e-cigarette use was significantly associated with the intention to smoke cigarettes (AOR, 1.17; 95% CI, 1.12–2.46) and waterpipes (2.63, 1.77–3.91). Current use also significantly increased odds of ever (15.09, 7.35–30.97), experimented (11.54, 5.26–25.32), quit (16.58, 7.07–38.91) and current tobacco smoking status (45.02, 19.24–105.38). Moreover, current e-cigarette use was significantly associated with cigarette (AOR: 1.73, 1.02–2.96), waterpipe (AOR: 3.71, 1.82–7.57) and other tobacco product dual use (13.83, 9.56–20.02) [Table 13].

Regarding the temporality and effects of e-cigarette use on cigarette smoking, 38.7% of those who had ever tried both cigarettes and e-cigarettes stated that they used e-cigarettes first. Out of all of the reasons to start smoking cigarettes, 21.0% believed that e-cigarette use caused their cigarette smoking. As for the effect of e-cigarette use on cigarette smoking, 58.8% of respondents reported no change or increased cigarette smoking after using e-cigarettes. Only 23.1% quit smoking and 18.1% smoked fewer cigarettes [Table 14].

Although e-cigarettes are marketed as a smoking cessation aid, using e-cigarettes in addition to cigarettes, as compared to just smoking cigarettes, did not show any significant difference in quitting intention (AOR, 1.02; 95% CI, 0.54–1.91). Negative but non-significant associations were shown in number of quit attempts in the past 12 months (0.88, 0.76–1.02), total number of quit attempts (0.95, 0.83–1.09) and duration of the longest

Table 6: Association of perceptions of e-cigarettes with e-cigarette use and intention of use

	Intention to use e-cigarettes in next 12 month					
	No intention		Intention to use		p-value from χ^2 test	AOR (95% CI)
	n	%	n	%		
Views on e-cigarettes					.000*	
Negative	18518	77.4%	466	23.5%		
Neutral or positive	5407	22.6%	1514	76.5%		11.275 (9.917–12.818)*
Beliefs on e-cigarette harms					.000*	
Not harmful	1959	8.1%	657	29.3%		4.868 (4.287–5.477)*
Harmful	22270	91.9%	1588	70.7%		
Beliefs on e-cigarette benefits						
Fewer harms					.000*	
No	4997	64.0%	245	33.7%		
Yes	2814	36.0%	481	66.3%		3.513 (2.886–4.277)*
Easier to buy/ more convenient					.000*	
No	6121	78.4%	411	56.6%		
Yes	1690	21.6%	315	43.4%		2.720 (2.254–3.282)*
More environmentally friendly/ clean					.000*	
No	6437	82.4%	481	66.3%		
Yes	1374	17.6%	245	33.7%		2.364 (1.948–2.868)*
More attractive/trendy					.000*	
No	6949	89.0%	494	68.0%		
Yes	862	11.0%	232	32.0%		3.721 (3.044–4.548)*
Easier to use unnoticed at home/school					.000*	
No	7326	93.8%	598	82.4%		
Yes	485	6.2%	128	17.6%		3.281 (2.559–4.207)*
Better accepted by parents/school					.000*	
No	7615	97.5%	623	85.8%		
Yes	196	2.5%	103	14.2%		6.032 (4.525–8.039)*
None of the above					.000*	
No	4878	62.5%	616	84.8%		
Yes	2933	37.5%	110	15.2%		0.299 (0.232–0.386)*
Perception on legality of e-cigarettes use in non-smoking areas					.000*	
Illegal	4110	45.7%	205	27.0%		1.000
Legal	2378	26.5%	251	33.1%		1.876 (1.496–2.353)*
Do not know	2499	27.8%	302	39.8%		2.327 (1.871–2.894)*

Table 7: Association of e-cigarette usage with respiratory symptoms

	Respiratory symptoms			
	No	Yes	p-value	AOR (95% CI)
	%	%		
All students	76.8%	23.2%		
E-cigarette use			0.000*	
Never used	77.4%	22.6%		1.00
Ever used	70.7%	29.3%	0.000*	1.36 (1.22–1.53)*
Used once or a few times	72.5%	27.5%	0.001*	1.29 (1.11–1.48)*
Used to use occasionally, but have quit now	71.7%	28.3%	0.049*	1.28 (1.00–1.64)*
Used to use every day, but have quit now	58.3%	41.7%	0.000*	2.16 (1.45–3.23)*
Current use	65.6%	34.4%	0.008*	1.59 (1.13–2.23)*
Occasionally use	63.7%	36.3%	0.084	1.54 (0.94–2.51)
Use every day	67.5%	32.5%	0.023*	1.74 (1.08–2.80)*

Table 8: Association of e-cigarette usage with perceived health status

	Perceived health status			
	Good to excellent	Fair to poor	p-value	AOR (95% CI)
	%	%		
All students	84.9%	15.1%		
E-cigarette use			0.000*	
Never used	85.8%	14.2%		1.00
Ever used	75.2%	24.8%	0.000*	1.33 (1.14–1.56)*
Used once or a few times	78.7%	21.3%	0.032*	1.22 (1.02–1.45)*
Used to use occasionally, but have quit now	74.3%	25.7%	0.007*	1.48 (1.11–1.96)*
Used to use every day, but have quit now	66.9%	33.1%	0.003*	1.96 (1.25–3.05)*
Current use	60.7%	39.3%	0.018*	1.57 (1.08–2.27)*
Occasionally use	69.0%	31.0%	0.185	1.43 (0.84–2.42)
Use every day	52.5%	47.5%	0.000*	2.49 (1.50–4.14)*

Table 9: Health effects of passive e-cigarette smoke exposure in never-users

Number of days of passive e-cigarette smoke exposure at home in the past 7 days

	p-value from χ^2 test	AOR (95% CI)	β
Perceived health status	.001*		
Fair or poor		1.12 (1.07–1.17)*	0.089
Good to excellent		1.00	
Respiratory symptoms in the past 12 months	.000*		
Yes		1.02 (0.97–1.06)	0.016
No		1.00	

Number of days of passive e-cigarette smoke exposure outside home in the past 7 days

	p-value from χ^2 test	AOR (95% CI)	β
Perceived health status	.000*		
Fair or poor		1.12 (1.08–1.16)*	0.078
Good to excellent		1.00	
Respiratory symptoms in the past 12 months	.000*		
Yes		1.05 (1.01–1.08)*	0.013
No		1.00	

Table 10: Comparison of general perception of e-cigarette and cigarette

	E-cigarettes		Cigarettes		p-value
	n	%	n	%	
Harms					.000*
Not harmful	2639	9.9%	1339	5.0%	
Harmful	23964	90.1%	25276	95.0%	
Views					.000*
Negative	19172	72.9%	21760	81.8%	
Neutral or Positive	7117	27.1%	4846	18.2%	

quit attempt (0.99, 0.92–1.08) in dual users compared with just cigarette smokers [Table 15].

Discussion

Current situation

The prevalence of past-30-day use (3.0%) and ever-use (8.9%) of e-cigarettes among Hong Kong secondary school students in 2016/17 were low compared with most Western countries. During the same time period, 11.3% of US high school students,[9] 25% of those aged 11–15 in England[10] and 6.3% of Canadians aged 15–19 used e-cigarettes in the past 30 days.[11] Ever-use of e-cigarettes was 27.1% in US adolescents,[12] 20.0% in New Zealand,[13] 7.1% in Australia[14] and 7–18% across the UK.[15] As for Asian countries, e-cigarette ever-use among adolescents was also higher in Japan[16] and Korea (9.4%),[17] but lower in China (3.1%) and Taiwan (2.2%).[18,19]

Table 11: Comparison of health between cigarette and e-cigarette users

	Current Use				p-value from χ^2 test	AOR (95% CI)
	E-cigarette user		Cigarette User			
	n	%	n	%		
Perceived health status					.039*	
Fair or poor	26	27.4%	252	38.3%		1.49 (0.90–2.46)
Good to excellent	69	72.6%	406	61.7%		1.00
Respiratory symptoms in the past 12 months					0.136	
Yes	29	31.2%	253	39.2%		1.59 (0.97–2.62)
No	64	68.8%	392	60.8%		1.00

Table 12: Relationship between e-cigarette and other tobacco products

All secondary school students		E-cigarette smoking status							
		Never		Experimented		Quit		Current	
		n	%	n	%	n	%	n	%
Cigarette smoking status	Never	22344	92.5%	642	44.2%	145	22.2%	19	7.9%
	Experimented	1318	5.5%	410	28.2%	124	19.0%	25	10.4%
	Quit	326	1.3%	206	14.2%	219	33.5%	50	20.7%
	Current	170	0.7%	195	13.4%	165	25.3%	147	61.0%
Use of tobacco products in past 30 days	Never	23622	97.60%	1117	76.30%	297	45.20%	38	15.50%
	Cigarettes	278	1.10%	264	18.00%	167	25.40%	94	38.40%
	Waterpipe	36	0.10%	43	2.90%	84	12.80%	47	19.20%
	Other	122	0.50%	80	5.50%	169	25.70%	146	59.60%

Table 13: Association of e-cigarette use with smoking intention and status

	E-cigarette use			
	Non-users	Current users	p-value from χ^2 test	AOR (95% CI)
	%	%		
Cigarette smoking intention in next 12 months			.000*	
Yes	3.6%	56.8%		1.17 (1.18–2.46)*
No	96.4%	43.2%		1.00
Waterpipe use intention in next 12 months			.000*	
Yes	2.9%	55.2%		2.63 (1.77–3.91)*
No	97.1%	44.8%		1.00
Smoking status				
Never smoked	88.1%	7.9%		1.000
Ever smoked	11.9%	92.1%	.000*	15.09 (7.35–30.97)*
Experimented	7.10%	10.4%	.000*	11.54 (5.26–25.32)*
Quit	2.9%	20.7%	.000*	16.58 (7.07–38.91)*
Current	2.0%	61.0%	.000*	45.02 (19.24–105.38)*
Use of tobacco products in past 30 days				
Never	95.20%	15.50%	0.182	0.47 (0.16–1.42)
Cigarettes	2.70%	38.40%	.000*	1.73 (1.02–2.96)*
Waterpipe	0.60%	19.20%	.000*	3.71 (1.83–7.57)*
Other tobacco products	1.40%	59.60%	.000*	13.83 (9.56–20.02)*

However, the past-30-day use prevalence (3.0%) in 2016/17 indicates a 272% increase from 1.1% in 2012/13.[7] The tripling of e-cigarette use in youth reflects a global pattern seen in other countries, including the US,[5] Canada,[11] Poland[20] and New Zealand.[13] Moreover, substantial growth in e-cigarette use opposes the decline of cigarette smoking in Hong Kong over the past few decades, which is among the lowest globally at 10.0%.[21] To illustrate, e-cigarettes have overtaken cigarettes as the most popular smoking device among teenagers in the US in 2019, with youth usage skyrocketing by 78% within 1 year.[22] This trend will likely be echoed in Hong Kong if this emerging device is not regulated.

Moreover, almost one in three e-cigarette users had their first e-cigarette puff during primary school age (≤11 years

old), which concurs with a local study showing a striking 55% increase in Primary 2–4 pupils who had used e-cigarette within a year.[7] These results are particularly concerning as those who started e-cigarettes early were more likely to be current and frequent users, use nicotine-containing e-cigarettes and other tobacco products. This will likely extend into adulthood and have severe impacts on their short-term and long-term health.

Table 14: Temporality and effect of e-cigarette use on cigarette smoking

	n	%
Temporality of cigarette and e-cigarette use		
E-cigarette first	796	38.7%
Cigarette first	1260	61.3%
Perception on whether e-cigarette use caused cigarette smoking		
Yes	366	21.0%
No	1379	79.0%
Change in smoking conventional cigarettes after using e-cigarettes		
Quit cigarettes	305	23.1%
Smoked fewer cigarettes	238	18.1%
Smoked more cigarettes	137	10.4%
No change	638	48.4%

Health effects

In Hong Kong, secondary school students who had ever-used, quit or currently use e-cigarettes were significantly more likely to have poorer perceived health than never-users, after adjusting for confounders including smoking status. All levels of e-cigarette use also significantly increased respiratory symptoms, corroborating with earlier local findings that showed significant associations between past-30-day use and respiratory symptoms.[23] This adds to existing evidence of increased cough, wheezing and asthma exacerbations in adolescent e-cigarette users.[24-27] Findings are also coherent across animal and in-vitro systems,[28] which suggest that respiratory symptoms are likely associated with increased oxidative stress, cellular inflammation, suppressed cough reflexes and impaired muco-ciliary clearance induced by e-cigarette aerosols.[29-34]

These results bolster the mounting evidence regarding the health risks of e-cigarettes. E-cigarettes have previously been endorsed by Public Health England[35] and the Royal College of Physicians[36] as harm reduction tools with 95% lower risk than smoking,[37] which explains the more positive perceptions of e-cigarettes among secondary school students. However, these findings have since been

Table 15: Association of cigarette and e-cigarette usage with quitting intention

	Current usage of cigarettes and e-cigarettes			
	Just cigarette smoker	Dual User	p-value from χ^2 test	AOR (95% CI)
	%	%		
Intention to quit smoking			0.961	
No	55.5%	58.0%		1.02 (0.54–1.91)
Yes	44.5%	42.0%		
Number of quit attempts in the past 12 months			.014*	0.88 (0.76–1.02)
0	30.3%	26.4%		
1	14.5%	27.8%		
2	14.9%	13.9%		
3 - 4	16.1%	8.3%		
5 - 9	5.6%	11.1%		
10 or more	18.6%	12.5%		
Total number of quit attempts			0.328	0.95 (0.83–1.09)
0	27.6%	22.8%		
1	14.8%	22.8%		
2	15.3%	17.7%		
3 - 4	16.0%	12.7%		
5 - 9	7.5%	10.1%		
10 or more	18.9%	13.9%		
Duration of the longest quit attempt			0.130	0.99 (0.92–1.08)
Smoke but never tried to quit	22.0%	13.2%		
Less than 1 day	10.2%	17.1%		
1 - 2 days	10.4%	10.5%		
3 - 4 days	8.7%	13.2%		
5 - 7 days	8.0%	2.6%		
8 - 13 days	6.1%	7.9%		
2 weeks to less than 1 month	7.8%	5.3%		
1 to less than 2 months	6.8%	6.6%		
2 months or longer	20.1%	23.7%		

criticized for drawing conclusions based on inadequate evidence, and no significant difference between Hong Kong secondary-school cigarette and e-cigarette users was found regarding their perceived health status and respiratory symptoms. Although exposure to certain toxic ingredients commonly found in cigarettes is indeed lower in e-cigarettes,[38-42] this does not mean that e-cigarettes are safe as general consumer products.

E-cigarette liquids and aerosols contain numerous toxic substances, including several known carcinogens (e.g. formaldehyde, acrolein) that support the possibility of increase cancer risk and adverse reproductive outcomes from long-term exposure.[43-47] Nicotine exposures are comparable to combustible tobacco cigarettes,[44,48] which leads to nicotine addiction and damages the developing adolescent brain.[5] Moreover, the number of heavy-metals, which are established to be highly toxic for multiple organ systems when inhaled,[28] are greater in e-cigarette aerosols than in tobacco-cigarettes.[49] Emerging evidence further demonstrates that e-cigarette usage increases the risk of long-term health outcomes, including emphysema, chronic bronchitis and COPD,[50] stroke,[9] myocardial infarction,[51] angina and coronary heart disease,[52] with a low probability of reverse causation.[9] The biological plausibility of these long-term health consequences are supported by new research showing decreased production in nitric oxide that protect blood vessels,[53] increased platelet function and thrombogenesis,[54] along with existing evidence that arterial stiffness, blood pressure and heart rate increase shortly after e-cigarette use.[55-58]

Passive e-cigarette smoke exposure at home and outside were shown to negatively affect perceived health status and respiratory symptoms in secondary school students who never used e-cigarettes. Second-hand e-cigarette emissions contribute to indoor air pollution above WHO recommended levels, although less so than second-hand tobacco smoke. The chemical cocktail of nicotine, diacetyl flavourings which are linked to serious respiratory diseases, ultra-fine particles, volatile organic compounds and heavy metals from second-hand emissions can adversely affect health, especially in children, pregnant women, elderly and cardiorespiratory disease patients.[28]

Gateway to tobacco

Regarding the association between e-cigarettes and tobacco-products, current adolescent e-cigarette use was significantly associated with increased intentions of tobacco smoking and waterpipe use in the next 12 months, cigarette smoking status (including those who ever-smoked, experimented, quit and currently smoke), and waterpipe and other tobacco product use in the past 30 days. Moreover, 2 in 5 of those who ever tried both cigarettes and e-cigarettes said they used e-cigarettes before cigarettes, and 21% believed that e-cigarette use caused their cigarette smoking. These findings all support e-cigarettes as a gateway to youth smoking and other tobacco product use, in line with large scale systematic reviews and studies conducted locally and abroad.[59-65] The majority of respondents also reported no change or increases in cigarette smoking after e-cigarette use, rather than reducing or quitting smoking. Positive correlation between e-cigarette use and cigarette smoking frequency and intensity is also documented in literature, with subsequent analysis showing that adolescent non-smokers who used e-cigarettes with higher nicotine concentrations were subsequently more likely to smoke more frequently.[66,67]

Smoking cessation

Despite being marketed as a smoking cessation tool, Hong Kong secondary school students who used e-cigarettes along with cigarettes did not show significant changes in quitting intention. Total number of quit attempts, number of quit attempts in the past year and duration of longest quit attempts were non-significantly lower in dual users than those who just smoked cigarettes. This supports WHO's decision to reject e-cigarettes as an effective smoking cessation tool, especially given that 'wanting to quit or reduce smoking' ranked among the least-cited reasons for using e-cigarettes in HK adolescents. Moreover, among current e-cigarette users, twice as many concurrently smoked cigarettes (61.0%) compared to those who experimented or quit smoking (31.1%), indicating dual use of e-cigarettes and cigarettes was much more likely than quitting smoking.

Conversely, a recent randomized trial showed that sustained abstinence was higher among e-cigarette users (18.0%) than nicotine-replacement therapy (9.9%), concluding that e-cigarettes are efficient smoking cessation tools.[68] However, upon further analysis, nicotine-free abstinence rates were in fact lower among e-cigarette users (3.7%) compared to those who received nicotine-replacement therapy (9.0%), with significant dual use among those who failed to quit. While there is no available data regarding the long-term health effects of dual use, it is likely that having two sources of nicotine can lead to effect multiplication on the harms.[5] Nonetheless, current evidence is inadequate to conclude that e-cigarettes are effective smoking cessation aids.[28] More research is needed to determine the effectiveness and feasibility of medicalising e-cigarettes as a restricted smoking cessation tool in Hong Kong.

Limitations and generalizability

There are various limitations to this study. First, the study was based on self-reported data which is subject to reporting biases. Second, the cross-sectional design does not permit causality inference on the temporal relationship between e-cigarette use and independent variables. Nonetheless, the large territory-wide, school-based sample and appraisal

of a wide range of factors affecting e-cigarette use in secondary school students suggest that these results can be generalizable to the Hong Kong adolescent population.

Conclusion

Overall, the tripling of e-cigarette use and substantial early initial in recent years is extremely concerning. This report does not support e-cigarettes as a harm reduction tool and shows that e-cigarettes are not safe as general consumer products. Moreover, their function as a gateway to smoking and reduction of quitting intention in adolescents may renormalize the tobacco industry and reverse all tobacco control efforts.[6] Above all, as the potential harms of e-cigarettes are not completely understood,[5] the precautionary principle should apply to protect the general public from exposures to the harms of e-cigarettes until further scientific findings emerge.[69]

The use of tobacco products, including e-cigarettes, continues to be a major health threat to children, adolescents and adults.[6] If the current trend of e-cigarette use among adolescents continues, the achievements in tobacco control would be completely undermined.[70] Given the unique role of paediatricians on influencing child and adolescent health in their early stages of development, paediatricians should counsel children and adolescents on the risks of e-cigarette use, and advise parents and caregivers who smoke or use e-cigarettes about quitting. Moreover, healthcare professionals should advocate for e-cigarette control policies to nip the growing e-cigarette epidemic in the bud. The proposed legislation to ban e-cigarette sales, distribution, importation, advertising and use in smoking-free areas should be passed as soon as possible to protect the health of our next generation.

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Conflicts of interest

There are no conflicts of interest.

References

1. Hong Kong Council on Smoking and Health. Smoking Prevalence for Males and Females in Hong Kong 2018. Available from: https://www.chp.gov.hk/en/healthtopics/content/25/8806.html# [Last accessed on 2022 May 17].
2. Caponnetto P, Campagna D, Papale G, Russo C, Polosa R. The emerging phenomenon of electronic cigarettes. Expert Rev Respir Med 2012;6:63-74.
3. Jones L. Vaping - the rise in five charts. BBC News. 2018. Available from: https://www.bbc.com/news/business-44295336. [Last accessed on 2022 May 17].
4. Hong Kong Council on Smoking and Health. Report on Tobacco Control Policy-related Survey 2017. 2017. [Available from: http://www.smokefree.hk/UserFiles/resources/about_us/cosh_reports/COSHRN_E24.pdf. [Last accessed on 2019 May 3].
5. Grana RA, Ling PM. "Smoking revolution": A content analysis of electronic cigarette retail websites. Am J Prev Med 2014;46:395-403.
6. Hong Kong Council of Smoking and Health. (June 2018) Press Release - Enact a total ban on e-cigarettes and other new tobacco products for the sake of public health. Available from: https://www.smokefree.hk/en/content/web.do?page=pr20180615. [Last accessed on 2019 May 3].
7. Jiang N, Wang MP, Ho SY, Leung LT, Lam TH. Electronic cigarette use among adolescents: A cross-sectional study in Hong Kong. BMC Public Health 2016;16:202.
8. National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General (US) AGCfDCaP, editor. 2016. Available from: https://www.cdc.gov/tobacco/data_statistics/sgr/e-cigarettes/index.htm. [Last accessed on 2022 May 17].
9. Ndunda PM, Muutu TM. Abstract 9: Electronic cigarette use is associated with a higher risk of stroke. Stroke 2019;50:A9.
10. Siddiqui F, Mishu M, Marshall AM, Siddiqi K. E-cigarette use and subsequent smoking in adolescents and young adults: A perspective. Expert Rev Respir Med 2019;13:403-5.
11. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Berenbaum E, KellerOlaman S, Manson H, Moloughney B, Muir S, Simms C, *et al*. Current evidence on ecigarettes: A summary of potential impacts. Toronto: Queen's Printer for Ontario; 2018.
12. Gentzke AS, Creamer M, Cullen KA, Ambrose BK, Willis G, Jamal A, *et al*. Vital Signs: Tobacco product use among middle and high school students — United States, 2011–2018. MMWR Morb Mortal Wkly Rep 2019;68:157-64.
13. White J, Li J, Newcombe R, Walton D. Tripling use of electronic cigarettes among New Zealand adolescents between 2012 and 2014. 2015;56:522-8.
14. Greenhalgh E, Scollo MM. InDepth 18B: Electronic cigarettes (e-cigarettes). In Scollo MM, Winstanley MH, editors. Tobacco in Australia: Facts and Issues. Melbourne: Cancer Council Victoria; 2017.
15. Bauld L, MacKintosh AM, Eastwood B, Ford A, Moore G, Dockrell M, *et al*. Young people's use of e-cigarettes across the United Kingdom: Findings from five surveys 2015–2017. Int J Environ Res Public Health 2017;14:973.
16. Lee S, Grana RA, Glantz SA. Electronic cigarette use among Korean adolescents: A cross-sectional study of market penetration, dual use, and relationship to quit attempts and former smoking. J Adolesc Health 2014;54:684-90.
17. Tabuchi T, Gallus S, Shinozaki T, Nakaya T, Kunugita N, Colwell B. Heat-not-burn tobacco product use in Japan: Its prevalence, predictors and perceived symptoms from exposure to secondhand heat-not-burn tobacco aerosol. Tob Control 2018;27:e25-33.
18. Chang HC, Tsai YW, Shiu MN, Wang YT, Chang PY. Elucidating challenges that electronic cigarettes pose to tobacco control in Asia: A population-based national survey in Taiwan. BMJ Open 2017;7:e014263.
19. Wang W, He Z, Feng N, Cai Y. Electronic cigarette use in China: Awareness, prevalence and regulation. Tob Induc Dis 2019;17:30.
20. Goniewicz ML, Gawron M, Nadolska J, Balwicki L, Sobczak A. Rise in electronic cigarette use among adolescents in Poland. J Adolesc Health 2014;55:713-5.
21. Hong Kong Council of Smoking and Health. COSH and Health Professionals Strongly Request for a Total Ban of Electronic Cigarettes.

News Update 2018. Available from: https://www.smokefree.hk/page.php?id=581&lang=en. [Last accessed on 2022 May 17].
22. Simon S. FDA Proposes Regulations as Teen E-Cigarette Use Skyrockets 78% in 1 Year. American Cancer Society 2018. Available from: https://www.cancer.org/latest-news/fda-proposes-regulations-as-teen-e-cigarette-use-skyrockets-78-percent-in-1-year.html#. [Last accessed on 2022 May 17].
23. Wang MP, Ho SY, Leung LT, Lam TH. Electronic cigarette use and respiratory symptoms in chinese adolescents in hong kong. JAMA Pediatr 2016;170:89-91.
24. Cho JH, Paik SY. Association between electronic cigarette use and asthma among high school students in South Korea. Plos One 2016;11:e0151022.
25. Choi K, Bernat D. E-cigarette use among Florida youth with and without asthma. Am J Prev Med 2016;51:446-53.
26. Kumral TL, Saltürk Z, Yildirim G, Uyar Y, Berkiten G, Atar Y, *et al*. How does electronic cigarette smoking affect sinonasal symptoms and nasal mucociliary clearance? B-Ent 2016;12:17-21.
27. McConnell R, Barrington-Trimis JL, Wang K, Urman R, Hong H, Unger J, *et al*. Electronic cigarette use and respiratory symptoms in adolescents. Am J Respir Crit Care Med 2017;195:1043-9.
28. National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on the Review of the Health Effects of Electronic Nicotine Delivery Systems. In: Eaton DL, Kwan LY, Stratton K, editors. Public Health Consequences of E-Cigarettes. Washington, DC: National Academies Press; 2018.
29. Husari A, Shihadeh A, Talih S, Hashem Y, El Sabban M, Zaatari G. Acute exposure to electronic and combustible cigarette aerosols: Effects in an animal model and in human alveolar cells. Nicotine Tob Res 2016;18:613-9.
30. Hwang JH, Lyes M, Sladewski K, Enany S, McEachern E, Mathew DP, *et al*. Electronic cigarette inhalation alters innate immunity and airway cytokines while increasing the virulence of colonizing bacteria. J Mol Med (Berl) 2016;94:667-79.
31. Laube BL, Afshar-Mohajer N, Koehler K, Chen G, Lazarus P, Collaco JM, *et al*. Acute and chronic in vivo effects of exposure to nicotine and propylene glycol from an E-cigarette on mucociliary clearance in a murine model. Inhal Toxicol 2017;29:197-205.
32. Lerner CA, Sundar IK, Yao H, Gerloff J, Ossip DJ, McIntosh S, *et al*. Vapors produced by electronic cigarettes and e-juices with flavorings induce toxicity, oxidative stress, and inflammatory response in lung epithelial cells and in mouse lung. PLoS One 2015;10:e0116732.
33. Lim HB, Kim SH. Inhallation of e-cigarette cartridge solution aggravates allergen-induced airway inflammation and hyper-responsiveness in mice. Toxicol Res 2014;30:13-8.
34. Sussan TE, Gajghate S, Thimmulappa RK, Ma J, Kim JH, Sudini K, *et al*. Exposure to electronic cigarettes impairs pulmonary anti-bacterial and anti-viral defenses in a mouse model. PLoS One 2015;10:e0116861.
35. McNeill A, Brose LS, Calder R, Hitchman SC. E-cigarettes: An Evidence Update: A Report Commissioned by Public Health England. London: Public Health England; 2015.
36. Royal College of Physicians of London. RCP Statement on E-cigarettes. London: Royal College of Physicians; 2014.
37. McKee M, Capewell S. Evidence about electronic cigarettes: A foundation built on rock or sand? BMJ 2015;351:h4863.
38. Canistro D, Vivarelli F, Cirillo S, Babot Marquillas C, Buschini A, Lazzaretti M, *et al*. E-cigarettes induce toxicological effects that can raise the cancer risk. Sci Rep 2017;7:2028.
39. Gillman IG, Kistler KA, Stewart EW, Paolantonio AR. Effect of variable power levels on the yield of total aerosol mass and formation of aldehydes in e-cigarette aerosols. Regul Toxicol Pharmacol 2016;75:58-65.
40. Kosmider L, Sobczak A, Fik M, Knysak J, Zaciera M, Kurek J, *et al*. Carbonyl compounds in electronic cigarette vapors: Effects of nicotine solvent and battery output voltage. Nicotine Tob Res 2014;16:1319-26.
41. Papoušek R, Pataj Z, Nováková P, Lemr K, Barták P. Determination of acrylamide and acrolein in smoke from tobacco and e-cigarettes. Chromatographia 2014;77:1145-51.
42. Tayyarah R, Long GA. Comparison of select analytes in aerosol from e-cigarettes with smoke from conventional cigarettes and with ambient air. Regul Toxicol Pharmacol 2014;70:704-10.
43. Bekki K, Uchiyama S, Ohta K, Inaba Y, Nakagome H, Kunugita N. Carbonyl compounds generated from electronic cigarettes. Int J Environ Res Public Health 2014;11:11192-200.
44. Goniewicz ML, Boykan R, Messina CR, Eliscu A, Tolentino J. High exposure to nicotine among adolescents who use juul and other vape pod systems ('pods'). Tob Control 2019;28:676-7.
45. Hess CA, Olmedo P, Navas-Acien A, Goessler W, Cohen JE, Rule AM. E-cigarettes as a source of toxic and potentially carcinogenic metals. Environ Res 2017;152:221-5.
46. Jensen RP, Luo W, Pankow JF, Strongin RM, Peyton DH. Hidden formaldehyde in e-cigarette aerosols. N Engl J Med 2015;372:392-4.
47. Uchiyama S, Ohta K, Inaba Y, Kunugita N. Determination of carbonyl compounds generated from the E-cigarette using coupled silica cartridges impregnated with hydroquinone and 2,4-dinitrophenylhydrazine, followed by high-performance liquid chromatography. Anal Sci 2013;29:1219-22.
48. Jackler RK, Ramamurthi D. Nicotine arms race: JUUL and the high-nicotine product market. Tobacco Control 2019;28:623-8.
49. Olmedo P, Goessler W, Tanda S, Grau-Perez M, Jarmul S, Aherrera A, *et al*. Metal concentrations in e-cigarette liquid and aerosol samples: The contribution of metallic coils. Environ Health Perspect 2018;126:027010.
50. Perez MF, Atuegwu N, Mead E, Oncken C, Mortensen EM. E-cigarette use is associated with emphysema, chronic bronchitis and COPD. Am J Respir Crit Care Med 2018;197:A6245.
51. Qasim H, Karim ZA, Rivera JO, Khasawneh FT, Alshbool FZ. Impact of electronic cigarettes on the cardiovascular system. J Am Heart Assoc 2017;6:e006353.
52. Glantz SA, Bareham DW. E-cigarettes: Use, effects on smoking, risks, and policy implications. Annu Rev Public Health 2018;39:215-35.
53. American Heart Association. Study: E-cigarettes may damage blood vessels. American Heart Association News Stories 2018. Available from: https://www.heart.org/en/news/2018/11/05/study-ecigarettes-may-damage-the-heart. [Last accessed on 2022 May 17].
54. Qasim H, Karim ZA, Silva-Espinoza JC, Khasawneh FT, Rivera JO, Ellis CC, *et al*. Short-term e-cigarette exposure increases the risk of thrombogenesis and enhances platelet function in mice. J Am Heart Assoc 2018;7:e009264.
55. Farsalinos K, Cibella F, Caponnetto P, Campagna D, Morjaria JB, Battaglia E, *et al*. Effect of continuous smoking reduction and abstinence on blood pressure and heart rate in smokers switching to electronic cigarettes. Intern Emerg Med 2016;11:85-94.
56. Moheimani RS, Bhetraratana M, Yin F, Peters KM, Gornbein J, Araujo JA, *et al*. Increased cardiac sympathetic activity and oxidative stress in habitual electronic cigarette users: Implications for cardiovascular risk. JAMA Cardiol 2017;2:278-84.
57. Polosa R, Morjaria JB, Caponnetto P, Battaglia E, Russo C, Ciampi C, *et al*. Blood pressure control in smokers with arterial hypertension who switched to electronic cigarettes. Int J Environ Res Public Health 2016;13:1123.
58. St Helen G, Dempsey DA, Havel CM, Jacob P 3rd, Benowitz NL. Impact of e-liquid flavors on nicotine intake and pharmacology of e-cigarettes. Drug Alcohol Depend 2017;178:391-8.
59. Etter JF. Gateway effects and electronic cigarettes. Addiction 2018;113:1776-83.
60. Hammond D, Reid JL, Cole AG, Leatherdale ST. Electronic cigarette use and smoking initiation among youth: A longitudinal cohort study. CMAJ 2017;189:E1328-36.
61. Kong G, Morean ME, Cavallo DA, Camenga DR, Krishnan-Sarin S. Reasons for electronic cigarette experimentation and discontinuation among adolescents and young adults. Nicotine Tob Res 2015;17:847-54.
62. Leventhal AM, Strong DR, Kirkpatrick MG, Unger JB, Sussman S, Riggs NR, *et al*. Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. JAMA 2015;314:700-7.

63. Lydon DM, Wilson SJ, Child A, Geier CF. Adolescent brain maturation and smoking: What we know and where we're headed. Neurosci Biobehav Rev 2014;45:323-42.
64. Schneider S, Diehl K. Vaping as a catalyst for smoking? An initial model on the initiation of electronic cigarette use and the transition to tobacco smoking among adolescents. Nicotine Tob Res 2016;18:647-53.
65. Wang MP, Ho SY, Leung LT, Lam TH. Electronic cigarette use and its association with smoking in Hong Kong chinese adolescents. Addict Behav 2015;50:124-7.
66. Leventhal AM, Stone MD, Andrabi N, Barrington-Trimis J, Strong DR, Sussman S, *et al*. Association of e-cigarette vaping and progression to heavier patterns of cigarette smoking. JAMA 2016;316:1918-20.
67. Wills TA, Sargent JD, Gibbons FX, Pagano I, Schweitzer R. E-cigarette use is differentially related to smoking onset among lower risk adolescents. Tob Control 2016;26:534-9.
68. Hajek P, Phillips-Waller A, Przulj D, Pesola F, Myers Smith K, Bisal N, *et al*. A randomized trial of E-cigarettes versus nicotine-replacement therapy. N Engl J Med 2019;380:629-37.
69. Read R, O'Riordan T. The precautionary principle under fire, environment. Sci Policy Sust Dev 2017;59:5,4-15.
70. Morean ME, Butler ER, Bold KW, Kong G, Camenga DR, Cavallo DA, *et al*. Preferring more e-cigarette flavors is associated with e-cigarette use frequency among adolescents but not adults. PLoS One 2018;13:e0189015-e.

Original Article

Correlation between Parental Knowledge Regarding Components of Written Asthma Action Plans and Asthma Control Levels in Asthmatic Children in Southern Taiwan

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Abstract

Background: Under the hypothesis that poor asthma control in Taiwan is associated with the underuse of written asthma action plans (WAAPs), we investigate the relationship between parental knowledge of key components of WAAP and asthma control levels. **Materials and Methods:** We conducted a prospective study from July 2019 to July 2021. "Written Asthma Action Plan" questionnaires were completed by the parents of asthmatic children, and the responses were correlated to the asthma symptom control level according to the Global Initiative for Asthma guidelines. **Results:** A total of 67 asthmatic children were enrolled (males 71.6%, mean age 6.3 ± 3.3 years). The asthma control level was significantly related to WAAP questionnaire score. The key components of "know the daily medication and how to use them" and "know the triggers and how to deal with them" both showed significantly higher understanding rates in the partly controlled children compared to the uncontrolled children ($P < 0.005$). The rates of having WAAPs were both below 10% in these two groups. **Conclusion:** The asthma control level was significantly and positively related to the understanding of key WAAP components. The development of an easy-to-use WAAP and its use as a standard tool for asthmatic children is expected to greatly improve asthma control in Taiwan.

Keywords: Asthma, asthma action plan, asthma control level, children, knowledge

Introduction

Pediatric asthma is a common chronic disease which imposes a heavy burden on healthcare systems worldwide.[1-3] Asthma attacks and worsening lung functions greatly affect the quality of life. The strategies to treat asthma include developing a patient–doctor partnership, identifying and reducing exposure to risk factors, monitoring asthma control, and managing asthma exacerbations.[1,2] The aim of the partnership is to equip patients and caregivers with the knowledge to play a major role in the treatment plan by discussing asthma severity, setting treatment goals, and developing a self-management plan, all of which have been shown to be beneficial in reducing asthma morbidity both in adults and children.[4-7] The Global Initiative for Asthma (GINA) guidelines recommend that all children should be provided with a written asthma action plan (WAAP) according to an individual's clinic condition, and that this WAAP should include details of how to recognize and respond to signs of worsening asthma.[1,2,4,5]

Asthma involves complex mechanisms and has many endotypes and phenotypes. There are obvious differences

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in the clinical manifestations and corresponding medications between individuals, and therefore personalized self-management plans are recommended for all asthma patients.[6,8] A WAAP should include the following key components: usual asthma medications, when and how to increase inhaled medications and start oral corticosteroids based on symptoms and/or peak expiratory flow, how to deal with the triggers and how to access medical care if symptoms fail to respond.[1,5,6] The patients are educated to recognize the signs of an attack, how to relieve airflow obstruction, and how to control acute inflammation episodes with the early application of rescue therapy and adjusting the anti-inflammatory medications.[2,9] The use of a WAAP and self-management of asthma in children and adolescents have been shown to significantly improve lung function, and reduce school absences, activity limitations, emergency department visits, and night disturbances.[5,6]

Asthma is still the most common chronic disease in Taiwan, and there is potential to improve control. Under the hypothesis that poor asthma control is associated with the underuse of WAAPs, we investigated the relationship between knowledge of key WAAP components and asthma control in Taiwan.

Materials and Methods

In this prospective study, asthmatic children below 18 years of age visiting a pediatric pulmonology outpatient clinic at a reference center in a university-affiliated hospital between July 2019 and July 2021 were enrolled, who were diagnosed as asthma according to the Global Initiative for Asthma guidelines. The informed consents were obtained from parents. Asthmatic children coexistent with cardiovascular, neurologic, or chronic lung diseases were excluded. The parents of the children completed a "Written Asthma Action Plan" questionnaire. The clinical data of the children were collected and characterized according to asthma symptom control. The percentage of those using a WAAP and whether the parents understood the key components of WAAP were analyzed. The study protocol was approved by the hospital's Ethical Review Committee.

Levels of asthma symptom control

The children were divided into well-controlled asthma group, partly controlled asthma group (PCG), and uncontrolled asthma group (UCG) according to the GINA guidelines. The level of asthma symptom control was evaluated according to the following four clinical findings, with each being scored as 0 for "No" and 1 for "Yes": In the past four weeks, has the patient had "Daytime asthma symptoms more than twice/week?", "Any night waking due to asthma?", "SABA reliever for symptoms more than twice/week?", and "Any activity limitation due to asthma?" A total score of 0 was defined as well-controlled asthma; a score of 1 or 2 was defined as PCG; and a score of 3 or 4 was defined as UCG.

WAAP questionnaire

The WAAP questionnaire was designed to assess a caregiver's knowledge regarding the key components of a WAAP. Sex, age, asthma severity, GINA asthma symptom control level, and the WAAP questionnaire responses were recorded [Table 1]. The 15 questions were categorized into six components: 1) know the daily medication and how to use them, 2) know the emergency medication and how to use them, 3) identify and respond when the asthma gets worse, 4) identify and respond to an asthma attack, 5) know the triggers and how to deal with the them, and 6) contact information of the health care providers. Each question was scored 1 if the caregiver knew the knowledge and 0 if not. The WAAP questionnaire scores were compared between the different asthma control groups.

Statistical methods

Descriptive analysis was used to assess the distribution of variables, including the level of asthma symptom control and questionnaire scores. The chi-square test and Fisher's exact test were used to investigate correlations between categorical variables from the questionnaires with different asthma control status. The Mann-Whitney U test

Table 1: Characteristics of the asthmatic children according to level of asthma symptom control according to the GINA guidelines

Asthma control level	Well-controlled group	Partly controlled group	Uncontrolled group	P value
Case number (n)	5	33	29	
Age (years) (M±SD)	8.5±4.7	6.7±3.5	5.4±2.7	0.147
Male (n(%))	2(40.0)	26(78.8)	20(69.0)	0.401
Time since diagnosis (n(%))				0.053
<3 months	0(0.0)	4(12.1)	12(41.4)	
3–6 months	3(60.0)	4(12.1)	3(10.3)	
6–12 months	1(20.0)	3(9.1)	3(10.3)	
>12 months	1(20.0)	22(66.7)	11(37.9)	
Grade of severity (n(%))				0.096
Intermittent	1(20.0)	0(0.0)	0(0.0)	
Mild persistent	4(80.0)	27(81.8)	18(62.1)	
Moderate persistent	0(0.0)	6(18.2)	11(37.9)	

The p values indicate partly controlled group versus uncontrolled group.

was used to compare differences in WAAP questionnaire mean scores. SPSS was used for all statistical analyses (version 15 for Windows®, SPSS Corporation, Chicago).

Results

Patients and WAAP knowledge questionnaires

A total of 70 asthmatic children initially met the criteria, however, three eligible cases did not participate in this study due to the time-consuming of filling out the WAAP questionnaire and other personal reasons. Finally, 67 asthmatic children were enrolled [Table 1], of whom 71.6% were male, and the mean age was 6.3 ± 3.3 years. There were no significant differences between the asthma status groups in age, sex, time since the diagnosis, and grade of severity (P = 0.147; P = 0.401; P = 0.053; and P = 0.056, respectively). There were 5 (7.45%) children in the well-controlled group, 33 (49.3%) in the PCG, and 29 (43.3%) in the UCG. Sixty-seven WAAP questionnaires which had been completed by the caregivers of the children were collected. We only analyzed differences between the PCG and UCG, as the number of children in the well-controlled group was too small (n = 5) to analyze.

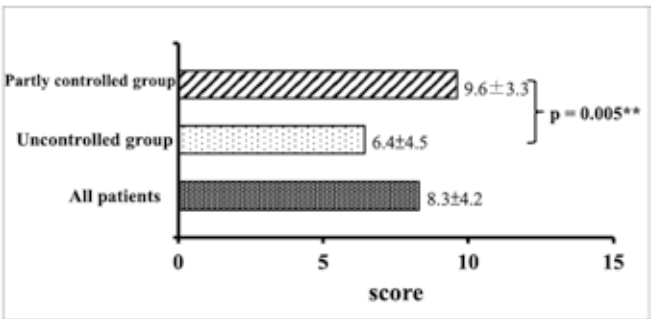

Figure 1: Mean WAAP questionnaire scores of the parents of all patients, partly controlled group, and uncontrolled group. **p value, partly controlled group versus uncontrolled group

Relationships between asthma control status and WAAP questionnaire score

The relationships between asthma control status and WAAP questionnaire score are shown in [Figure 1]. The asthma control level was significantly related to WAAP questionnaire score. The WAAP score in the PCG was significantly higher than that in the UCP, with 9.6 ± 3.3 in the PCG and 6.4 ± 4.5 in the UCP (P = 0.005)

Relationships between asthma control status and the understanding rate of items in the WAAP questionnaire

When we further analyzed the responses in the WAAP questionnaire, we found there were significant differences between the PCG and UCG in five items (P < 0.05, Table 2). These five items were: "know the anti-inflammatory medicine", "know the dose and frequency of anti-inflammatory medicine", "know the correct instructions

Table 2: The understanding rate (%) of each item in the WAAP questionnaire for all patients, partly controlled and uncontrolled asthma groups

Know the daily medications and how to use them (%)				
1. Know the anti-inflammatory medicine	74.2	87.9	58.6	0.018*
2. Know the dose and frequency of anti-inflammatory medicine	66.1	84.8	46.4	0.002*
3. Know the correct instructions of how to use the anti-inflammatory medicine	40.3	54.5	25.0	0.036*
Know the emergency medications and how to use them (%)				
4. Know the emergency medicine	64.5	75.8	51.7	0.065
5. Know the dose and frequency of the emergency medicine	35.5	43.8	27.6	0.286
6. Know the correct instructions of how to use the emergency medicine	27.4	36.4	17.2	0.153
Identify and respond when the asthma gets worse (%)				
7. Identify the symptoms when the asthma gets worse	77.4	84.8	69.0	0.223
8. Know how to respond when the asthma gets worse	33.9	45.5	20.7	0.060
Identify and respond to an asthma attack (%)				
9. Identify and respond to an asthma attack	75.8	81.8	69.0	0.373
10. Know how to respond when an asthma attack occurs	38.7	39.4	37.9	1.000
Know the triggers and how to deal with them (%)				
11. Know the predisposing factors	74.2	90.9	55.2	0.003*
12. Know the allergens	64.5	78.8	48.3	0.017*
13. Know how to prevent the predisposing factors	46.8	59.4	34.5	0.073
Contact information of the healthcare providers (%)				
14. Know how to contact the physician	56.5	63.6	48.3)	0.306
15. Know how to contact the nurse/educators	32.3	33.3	32.1	1.000

p values, partly controlled group versus uncontrolled group

Table 3: Utilization rate of WAAPs between the partly controlled and uncontrolled asthma groups

Patients	All (n=62)	Partly controlled group (n=33)	Uncontrolled group (n=29)	p
a.Know about WAAP (%)	27.4	33.3	20.7	0.393
b.Have your own WAAP (%)	4.8	9.1	0.0	0.241

p values, partly controlled group versus uncontrolled group.

of how to use the anti-inflammatory medicine", "know the predisposing factors", and "know the allergens". The first three items were in the "know daily asthma medication" component, and the last two items were in the "deal with the triggers" component.

Utilization rate of WAAPs between the partly controlled and uncontrolled asthma groups

Low understanding rates for "know about WAAP" and "have your own WAAP" were noted in both the PCG and UCG ($P > 0.05$), at only 33.3% and 9.1% in the PCG, and 20.7% and 0% in the UCG, respectively [Table 3].

Discussion

To evaluate the relationship between asthma control and strategy of WAAPs, we conducted a prospective questionnaire-based study and investigated the asthma control status and knowledge of WAAPs in Taiwan. We found a positive close relationship between knowledge regarding the key WAAP components and asthma control status, showing the importance of including WAAPs in the treatment strategy for pediatric asthma. Goronfolah *et al.* reported that WAAPs were effective in increasing the patients' knowledge about their condition, improving their quality of life and functional limitations, and increasing their confidence level about controlling their asthma.[10] In addition, Lakupoch *et al.* reported a significant reduction in emergent room visits, unscheduled outpatient department visits, admission days and school absence days in patients who used WAAPs.[11] Properly educating the patients and parents regarding knowledge of WAAPs has the potential to improve asthma control in Taiwan. In our study, there were significant differences in the understanding of knowledge in the "know the daily medications and how to use them" and "know the triggers and how to deal with them" components in the WAAP questionnaire between the PCG and UCG.

In the "know daily asthma medications" component, the PCG had significantly higher understanding rates of all three items than the UCG. This means that the caregivers of the children in the PCG had better understanding of "know the anti-inflammatory medicine", "know the dose and frequency of anti-inflammatory medicine", and "know the correct instructions of how to use the anti-inflammatory medicine", and this was related to better control of asthma. Anti-inflammatory agents are the main medications used to control the inflammatory status, and stabilize the condition after recovering from an asthma exacerbation. However, knowledge of medications, good drug compliance, and accurate use including the kind, dose, and inhalation technique is complex, time-consuming, and needs to be taught repeatedly. Bhupathi *et al.* reported that in spite of inhaled corticosteroids being effective in the management of asthma, oral medications and nebulizers are the mainstay treatment in the majority of the cases in India. Social stigma, fear of addiction, and lack of knowledge are the major reasons for the reluctance of parents towards the use of inhalers.[12] Using WAAPs to reinforce the comprehension and acceptance of inhaled corticosteroids, including the side effects and instructions, is important, and will lead to better control of asthma.

In this key component, the understanding rate of "know the correct instructions of how to use the anti-inflammatory medicine" was both unsatisfactory in both the PCG (54.5%) and UCG (25%). In Thailand, Pothirat *et al.* reported that inhalation techniques in asthma patients were mostly unsatisfactory, especially in those who had been treated by a pulmonologist for less than 2 years. They concluded that face-to-face training could significantly improve the technique for all devices.[13] Almomani *et al.* conducted a study of 150 pediatric asthma patients on the proper handling of asthma inhalers in 2019–2020, and found that correct technique rates of 13.4%, 38.5%, and 28.9% for Metered dose inhalers (MDI), Turbohaler, and Diskus, respectively. They also found that a higher number of correct MDI steps and fewer errors in critical steps were associated with a higher level of parental knowledge. Continuous education on appropriate inhaler techniques for asthmatic children is mandatory.[14]

In the "know the triggers and how to deal with them" component, the PCG had significantly higher understanding rates of "know the predisposing factors" and "know the allergens" than the UCG. This means that the caregivers of the children in the PCG had better understanding of these items, and this was related to better control of asthma. The first strategy to treat asthma is to know and avoid the predisposing factors. The most common predisposing factors are allergens, infections, exercise, emotional changes, medications, and temperature changes. Sensitization and allergens can be checked using blood tests and clinical correlations,[15] and the most common allergens are mites, dog hair, cat hair, cockroaches, house mites, fungi, chemical stimulants, seafood, eggs and milk.[15] Pathogens can be

identified through virus and blood tests for mycoplasma pneumonia.[16] The other predisposing factors can be assessed by the history of asthma exacerbations. In some situations, an allergen test or microorganism survey may not be performed. The predisposing factors are complex and easy to forget, and therefore it is preferable to write down the information rather than just telling them. WAAPs may act as a friendly reminder.

We also found that only 27.6% of parents knew about WAAP and 4.8% of children and parents had their own WAAP before this study. Both the PCG and UCG had low understanding rates for "know about WAAP" and "have your own WAAP" at only 33.3% and 9.1% in the PCG, and 20.7% and 0% in the UCG, respectively. The reasons for the infrequent use of WAAPs included too time consuming for doctors and difficult for parents to understand. In 2017, Lakupoch *et al.* conducted a prospective study using newly developed WAAPs in 49 children aged 5–18 years old with asthma, and found a significant decrease in emergency room visits after 6 months.[11] These newly developed WAAPs used pictures of asthma symptoms along with a simple format, and colorful pictures of all available medications and devices, which the authors concluded were easier to understand. Moreover, the WAAP was user-friendly, and the physicians could complete it within 5 minutes. A WAAP is an important tool to remind the patients to prevent the triggers, monitor themselves confidently, use controllers and relievers correctly, contact the healthcare providers as needed, and finally promote asthma control. It is important to improve the format of WAAPs by making them more user friendly and emphasize the benefits of using them so that they become the standard strategy to promote the quality of asthma care in children.

There are some limitations to this study. First, this is a cross-sectional study, and we studied the correlation between parental knowledge regarding components of WAAP and asthma control levels in asthmatic children at one clinic visit. We did not evaluate the effectiveness of the WAAP, since we did not follow-up the patients with regards to asthma symptom control level after a WAAP intervention. Second, because well-controlled asthma patients were transferred or chose to visit a local clinic, the number of well-controlled asthma patients was small, and therefore we only compared the PCG and UCG. Besides, during the COVID-19 pandemic, a relatively smaller number of patients searched the healthcare services in medical centers.

In conclusion, our results demonstrated that the asthma control level was significantly and positively related to the understanding status of key components in the WAAP questionnaire. Although a persistent high prevalence of pediatric asthma is noted in Taiwan, the utilization rate of WAAPs is very low. The development of an easy-to-use WAAP and its use as a standard tool for asthmatic children is expected to greatly improve asthma control in Taiwan.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Availability of data and material (data transparency)

The patients' data were collected during the presence at E-Da hospital. According to the regulation of E-Da Hospital Ethical Review Committee and the "Personal Information Protection Act" in Taiwan, patients' raw data cannot be made public. The interpretation of the analyzed results acquired from medical records been unlinked to patients' identification and is available from the corresponding author upon request of the editorial staff.

Code availability (software application or custom code)

Not applicable.

Authors' contributions

Yu-Cheng Tsai, Yu-Tsun Su and Ching-Chung Tsai conceptualized the study, collected grants, and wrote the initial paper; Yi-Pei Tai , Hsiu-Chuan Wang and Yuan-Yi Huang contributed to data collection and data analysis; Yuan-Yi Huang and Yu-Tsun Su contributed to the study design and edited the paper. All authors approved the final paper as submitted.

Ethics approval

The study protocol was approved by the E-Da Hospital Ethical Review Committee.

Consent to participate

All the participants signed the requirement of consent.

Consent for publication

The authors have agreed that the article be published by Pediatric Respirology and Critical Care Medicine.

References

1. Reddel HK, Boulet L-P. 2022 GINA Report, Global Strategy for Asthma Management and Prevention. *Global Initiative for Asthma*. 2022. https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf.
2. Bacharier LB, Boner A, Carlsen KH, Eigenmann PA, Frischer T, Götz M, *et al.*; European Pediatric Asthma Group. Diagnosis and treatment of asthma in childhood: A PRACTALL consensus report. Allergy 2008;63:5-34.

3. Bush A. Asthma: what's new, and what should be old but is not! Pediatr Respirol Crit Care Med 2017;1:2-10.
4. MacGillivray ME, Flavin MP. Canadian paediatric asthma action plans and their correlation with current consensus guidelines. Paediatr Child Health 2014;19:362-6.
5. Gibson PG, Powell H. Written action plans for asthma: An evidence-based review of the key components. Thorax 2004;59:94-9.
6. Guevara JP, Wolf FM, Grum CM, Clark NM. Effects of educational interventions for self management of asthma in children and adolescents: Systematic review and meta-analysis. BMJ 2003;326:1308-9.
7. Gibson PG, Powell H, Coughlan J, Wilson AJ, Abramson M, Haywood P, *et al*. Self-management education and regular practitioner review for adults with asthma. Cochrane Database Syst Rev 2003;1:CD001117.
8. Coté J, Cartier A, Robichaud P, Boutin H, Malo JL, Rouleau M, *et al*. Influence on asthma morbidity of asthma education programs based on self-management plans following treatment optimization. Am J Respir Crit Care Med 1997;155:1509-14.
9. Al-Muhsen S, Horanieh N, Dulgom S, Aseri ZA, Vazquez-Tello A, Halwani R, *et al*. Poor asthma education and medication compliance are associated with increased emergency department visits by asthmatic children. Ann Thorac Med 2015;10:123-31.
10. Goronfolah L, Abulaban A, Barnawi AI, Jawi M, Alhadhrami W, Baatiah NY. The effectiveness of written asthma action plan at the national guard health affairs' asthma clinic. Cureus 2019;11:e6247.
11. Lakupoch K, Manuyakorn W, Preutthipan A, Kamalaporn H. The effectiveness of newly developed written asthma action plan in improvement of asthma outcome in children. Asian Pac J Allergy Immunol 2018;36:88-92.
12. Bhupathi, S.D. and Vidhyasagar, *Beliefs and Factors Affecting the Usage and Compliance of Inhalers in Treatment of Asthma in Children*. Journal of Pharmaceutical Research International 2021 33:18-24.
13. Pothirat C, Chaiwong W, Limsukon A, Phetsuk N, Chetsadaphan N, Choomuang W, *et al*. Real-world observational study of the evaluation of inhaler techniques in asthma patients. Asian Pac J Allergy Immunol 2021;39:96-102.
14. Almomani BA, Al-Qawasmeh BS, Al-Shatnawi SF, Awad S, Alzoubi SA. Predictors of proper inhaler technique and asthma control in pediatric patients with asthma. Pediatr Pulmonol 2021;56:866-74.
15. Su YT, Yang YN, Li YC, Tsai CC, Chen LM, Lin YC, *et al*. Age-dependent distribution of the atopic phenotype and allergen sensitization among asthmatic children in southern taiwan. Asian Pac J Allergy Immunol 2016;34:206-11.
16. Su YT, Lin YT, Yang CC, Tsai SS, Wang JY, Huang YL, *et al*. High correlation between human rhinovirus type C and children with asthma exacerbations in taiwan. J Microbiol Immunol Infect 2020;53:561-8.

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LIBERTY ASTHMA QUEST Study Design*: 1902 patients who were 12 years of age or older with uncontrolled asthma were randomly assigned in a 2:2:1:1 ratio to receive add-on subcutaneous DUPIXENT at a dose of 200 or 300 mg every 2 weeks or matched-volume placebo for 52 weeks. The primary end points were the annualized rate of severe asthma exacerbations and the absolute change from baseline to week 12 in the forced expiratory volume in 1 second (FEV$_1$) before bronchodilator use in the overall trial population. Secondary end points included the exacerbation rate and FEV$_1$ in patients with a blood eosinophil count of 300 or more per cubic millimetre. Asthma control and DUPIXENT safety were also assessed.

EOS, eosinophilic; FeNO, fractional exhaled nitric oxide; ICS, inhaled corticosteroid; OCS, oral corticosteroid; Q2W, once every 2 weeks; SOC, standard of care

References: 1. DUPIXENT Summary of Product Characteristics, May 2020. **2.** Rabe KF, Nair P, Brusselle G, et al. Efficacy and safety of dupilumab in glucocorticoid-dependent severe asthma. N Engl J Med. 2018;378(26):2475-2485. **3.** Castro M, Corren J, Pavord ID, et al. Dupilumab Efficacy and Safety in Moderate-to-Severe Uncontrolled Asthma. N Engl J Med. 2018;378(26):2486-2496.

Presentation: Dupilumab solution for injection in a pre-filled syringe with needle shield. **Indications:** Atopic Dermatitis (AD): Moderate-to-severe AD in adults and adolescents ≥12 years who are candidates for systemic therapy; severe atopic dermatitis in children 6 to 11 years old who are candidates for systemic therapy. Asthma: In adults and adolescents ≥12 years, as add-on maintenance treatment for severe asthma with type 2 inflammation characterized by raised blood eosinophils and/or raised FeNO, who are inadequately controlled with high dose ICS plus another medicinal product for maintenance treatment. Chronic rhinosinusitis with nasal polyposis (CRSwNP): As an add-on therapy with intranasal corticosteroids for the treatment of adults with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control(for 300mg) **Dosage & Administration:** Subcutaneous injection. AD adults: initial dose of 600 mg (two 300 mg injections), followed by 300 mg every other week. AD adolescents(12-17y/o): Body weight <60kg: initial dose of 400 mg (two 200mg injections), followed by 200 mg every other week. Body weight ≥60 kg: same dosage as adults. Dupilumab can be used with or without topical corticosteroids. Topical calcineurin inhibitors may be used, but should be reserved for problem areas only, e.g. face, neck, intertriginous and genital areas. Consider discontinuing treatment in patients who have shown no response after 16 weeks. AD Children(6-11y/o): (Body weight 15Kg-<60 kg: initial dose of 300mg on Day 1 follow by 300mg on Day 15, then 300mg every 4 weeks. Body weight ≥60 kg: same dosage as adults. * The dose may be increased to 200 mg Q2W in patients with body weight of 15 kg - < 60 kg based on physician's assessment. Asthma: Initial dose of 400 mg, followed by 200 mg every other week. For patients with severe asthma and on oral corticosteroids or with severe asthma and co-morbid moderate to severe AD or adults with comorbid severe CRSwNP: Initial dose of 600 mg, followed by 300 mg every other week. Patients receiving concomitant oral corticosteroids may reduce steroid dose gradually once clinical improvement with dupilumab has occurred. The need for continued dupilumab therapy should be considered at least annually as determined by a physician. If a dose is missed, administer it asap and thereafter, resume dosing at the regular scheduled time. **Contraindications:** Hypersensitivity to dupilumab or any of the excipients. **Precautions:** Safety and efficacy in children <6 years or <15kg not been established. Not be used to treat acute asthma symptoms, acute exacerbations, acute bronchospasm or status asthmaticus. Do not discontinue corticosteroids abruptly upon start of dupilumab. Reduction should be gradual and performed under supervision of a physician; it may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy. Biomarkers of type 2 inflammation may be suppressed by systemic corticosteroid use. If systemic hypersensitivity reaction occurs, discontinue dupilumab and initiate appropriate therapy. Be alert to vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in patients with eosinophilia. Treat pre-existing helminth infections before initiating dupilumab. If patients become infected while receiving dupilumab and do not respond to anti-helminth treatment, discontinue dupilumab until infection resolves. Patients who develop conjunctivitis and keratitis that does not resolve following standard treatment should undergo ophthalmological examination. AD patients with comorbid asthma should not adjust or stop asthma treatments without consultation with physicians. Carefully monitor patients after discontinuation of dupilumab. Do not give live and live attenuated vaccines concurrently with dupilumab. Patients should be brought up to date with immunizations before starting dupilumab. **Drug interactions:** Immune responses to TdaP vaccine and meningococcal polysaccharide vaccine were assessed. Patients receiving dupilumab may receive concurrent inactivated or non-live vaccinations. **Pregnancy and lactation:** Should be used during pregnancy only if potential benefit justifies potential risk to foetus. Unknown whether dupilumab is excreted in human milk or absorbed systemically after ingestion. 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DUPIXENT® (dupilumab) Injection
200mg · 300mg