

The Epidemiology and Impact of Chronic Rhinosinusitis upon Populations in Seychelles: An analysis of data from primary health facilities across Mahé, Praslin and La Digue

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Background and significance

Chronic rhinosinusitis is considered to be an emerging health problem by the International Collaboration in Asthma, Allergy and Immunology, due to increases in prevalence and its marked socioeconomic impact upon individuals and societies, worldwide (Bachert et al., 2014). The condition is of inflammatory origin and typically characterised by symptoms of facial pain, discomfort or pressure, hyposmia or anosmia, nasal discharge and nasal obstruction; although most guidelines state that only two out of four of these symptoms are required to make a clinical diagnosis, formal diagnosis requires objective assessment using endoscopy or computed tomography in order to exclude differential diagnoses, such as migraine and upper respiratory tract infection (Desrosiers et al., 2011; Bhattacharyya and Lee, 2010; Fokkens et al., 2012). However in Seychelles, poor availability of diagnostic equipment and shortages of specialist Otorhinolaryngologists as a result of deficiencies and variances in the training of such physicians is likely to confound accurate chronic rhinosinusitis diagnosis – a problem that is largely absent among high income countries (Khan and Saeed, 2012). The chronicity of rhinosinusitis requires symptoms to have been present for at least 12 weeks and, notably, the condition is sometimes classified into two types based on the presence or absence of bilateral nasal polyps within the sinuses and/or middle meatus (Meltzer et al., 2004; Fokkens et al., 2012). Moreover, chronic rhinosinusitis can be classified using simple clinical criteria related to pain intensity using the Visual Analogue Scale with scores 0-3 indicating mild disease and >3-10 reflecting moderate to severe disease (Fokkens et al., 2012). Chronic rhinosinusitis is reported to have a heritability of 15-50%, with most cases being observed in persons with co-existing asthma and other allergic conditions, as well in those with cystic fibrosis, which has implicated the CFTR gene in the pathogenesis of the condition (Jani and Hamilos, 2005; Wang et al., 2000). The origins of chronic rhinosinusitis also interplay with epigenetic aberrations and environmental exposures, highlighting the complexity of pathogenesis, although cigarette smoking is the only known risk factor and there is little understanding whether isolated or multiple episodes of acute rhinosinusitis are sufficient to induce chronicity (Meltzer et al., 2004; Hastan et al., 2011).

The incidence and prevalence of chronic rhinosinusitis has been compounded by a lack of epidemiological studies with the available few having been conducted in Europe, Asia and North America, where the prevalence rate varies between 2-19% with a mean of 10.9% (Pleis, Ward and Lucas, 2010; Kim et al., 2011; DeConde and Soler, 2016). The impact of chronic rhinosinusitis, termed an unrecognized epidemic, is reflected in morbidity and service data showing that the chronic and unpleasant nature of symptoms markedly impairs quality of life to a degree comparable to other distressing ailments, including cancer, incontinence and acquired immunodeficiency syndrome, and accounts for healthcare costs in the order of \$8 billion per year, due to the high rate of medical consultations/advice, sinus surgery and medication (Tan et al., 2013; Schenkel et al., 2018). Other and wider costs to society due to chronic rhinosinusitis also arise from productivity losses due to absenteeism from work, as well as affected individuals observing a heightened risk of depression, which can exacerbate the complete burden of the condition through worsening physical function, mental wellbeing and quality of life (Schlosser et al., 2016). Although the prevalence and burden of chronic rhinosinusitis has been reported among several developing and developed nations, epidemiological trends are markedly under-reported for most other parts of the world, which has implications for the planning and evaluation of prevention and management strategies and impairs policy decision making concerning service and resource provision and allocation of funding (Hannaford, Smith and Elliott, 2005).

Indeed, the epidemiology of chronic rhinosinusitis affecting populations in Seychelles, an archipelago of more than 100 islands located within the Indian Ocean off the south eastern coast of Africa, is lacking but imminently required given anecdotes that the condition is rising in parallel with increases in respiratory tract infections. Notably, evidence from the Institute for Health Metrics and Evaluation has found that respiratory tract infections are one of the leading causes of premature mortality among the Seychellois population and, thus, a proportion of these infections and deaths may be attributed to chronic rhinosinusitis as a postulated initiating risk factor (Institute for Health Metrics and Evaluation, 2019). The data also revealed that respiratory tract infection related mortality had increased by more than 20% over the most recent decade and was only marginally preceded by cardiac disease, suggesting that it is one of the most burdensome problems affecting the health and wellbeing of Seychellois people (Institute for Health Metrics and Evaluation, 2019). Respiratory infections were also found to account for 15% of disability-adjusted life years; however, data concerning morbidity and mortality was not stratified aetiologically and, thus, the contribution of chronic rhinosinusitis to the former burden is currently unclear (Institute for Health Metrics and Evaluation, 2019). Notably, reverse causation between respiratory tract infections and chronic rhinosinusitis cannot be excluded and, thus, the common occurrence of clinically significant respiratory infections in Seychelles may predispose a substantial proportion of the population to developing chronic rhinosinusitis, which

could be better understood with the gathering of epidemiological data (Bose, Grammer and Peters, 2016).

Therefore, this research primarily aimed to collect and analyse epidemiological data concerning chronic rhinosinusitis across Seychelles, in order to address the clear knowledge gap. A secondary aim was to collect and analyse qualitative data from a small cohort of affected Seychellois persons, in order to better understand its impact upon individuals' everyday lives. It was hoped that the study could improve the burden and outcomes of chronic rhinosinusitis over time, particularly as epidemiological evidence could inform critical revisions to current rhinosinusitis guidelines which, at present, are non-specific – being limited to adults with acute, rather than chronic, rhinosinusitis and compromising empirical treatment recommendations that are not tailored to local practice and resource availability (Gluck et al., 2018). Moreover, the Seychellois government only spends 3.4% of its gross domestic product on healthcare, and considering this limited monetary capacity, it is essential that policy decision makers have sufficient and valid evidence to make appropriate and informed decisions regarding health expenditure – a factor that directly influences health outcomes and one that could be modified with evidence from this study to improve those associated with chronic rhinosinusitis (WHO, 2019a; WHO, 2019b).

Methods

A primary methodological approach in the form of a mixed-methods study was adopted to facilitate the evaluation of epidemiological data and trends of chronic rhinosinusitis in Seychelles, and to better understand the impact of the disease upon affected individuals' lives. The epidemiological component comprised a prospective analysis of data collected by primary health facilities across the three most populous islands, whilst the qualitative component consisted of a cross-sectional analysis of interview data. A positivist paradigm was adopted for the purpose of conducting this study, in order to ensure that the findings were interpreted and reported with objective realism and to minimise bias associated with researcher subjectivity (Aliyu et al., 2014).

The study was based on data collected from primary health centres located among the three most populous islands of Seychelles, Mahé, Praslin and La Digue, that represent 215 km² of the total 455 km² of Seychellois land mass; and these three islands are inhabited by an estimated 97,050 persons, which equates to 98% of the total population. Mahé is the largest Seychellois island with a land mass of 160 km² and comprising 85,462 persons or 87.5% of the entire population (population density 534/km²), followed by Praslin and La Digue with populations of 8,662 (density 216/km²) and 2,926 (density 195/km²), respectively. Other islands, including the inner and outer islands, were excluded for being either remotely or unclearly populated and/or under private ownership or restricted control. Based on census data, the population residing within

these areas was estimated to be less than 1,000 persons with a population density ranging between 0-2.7/km² (National Statistics Bureau, 2019b). Primary health centres within the main districts and areas of each of the three main islands were identified and selected as sources for data collection and evaluation. In Mahé, a total of 16 health centres were identified and data concerning chronic rhinosinusitis was included in this study and supplemented by data from three primary facilities within Praslin and La Digue. Health facilities in Mahé were located in the following districts/areas: Anse aux Pins, Anse Boileau, Anse Etoile, Anse Royale, Au Cap, Baie Lazare, Beau Vallon, Bel Ombre, Cascade, Glacis, Grand Anse, Perseverance, Pointe Larue, Port Glaud, Takamaka, and Victoria. Given that the islands of Praslin and La Digue are more sparsely populated, there were only three health facilities identified with two located in the Praslin regions of Baie Sainte Anne and Grand Anse, and one within the La Passe region of La Digue. The target sample comprised both children and adults who had received a documented clinical diagnosis of chronic rhinosinusitis by a primary care physician between March 2015 and March 2019. The documented diagnosis also had to meet formal clinical, but not objective, diagnostic criteria for rhinosinusitis as defined by the European Position Statement (Fokkens et al., 2012). This restriction was due to the poor availability and access to nasal endoscopy equipment and computed tomography scanners within Seychelles. The clinical criteria used for case ascertainment was as follows:

For adults, chronic rhinosinusitis was defined as:

- ♦ Inflammation of the nose and paranasal sinuses with nasal congestion/obstruction or nasal discharge for ≥ 12 weeks/3 months.
 - +/- Facial discomfort/pain/pressure
 - +/- Anosmia

For children, chronic rhinosinusitis was defined as:

- ♦ Inflammation of the nose and paranasal sinuses with nasal congestion/obstruction or nasal discharge for ≥ 12 weeks/3 months
 - +/- Facial discomfort/pain/pressure
 - +/- Cough

Data concerning the symptoms and duration of symptoms related to chronic rhinosinusitis, as well as patient demographics, past medical history, allergy history and smoking status, was collected for epidemiological analysis. Few primary health facilities within Seychelles have means for electronically recording and storing data concerning patient's health, with most of these being located within and around the capital of Victoria in Mahé. This meant that health data from these facilities could be searched and extracted for epidemiological analysis. For other districts/areas in Mahé, and health facilities among the islands of Praslin and La Digue, health data is recorded manually on physical paper records, and therefore all included facilities within these areas were contacted, and permission and compliance of resident primary physicians was sought, in order to permit derivation of a list of all case-note references of patients with suspected

and/or diagnosed rhinosinusitis. As the chronicity of rhinosinusitis was not always documented, all electronic and physical patient records were screened by the principal investigator and the symptoms and duration of rhinosinusitis were reviewed for eligibility in accordance with the former criteria, in order to generate case ascertainment. Data collection commenced in March 2015, that defined time zero, and continued prospectively to study-end, which was inclusive of March 2019. Data was collected at one-yearly intervals during the four-year study period and inputted into a secure and pre-developed electronic database to facilitate familiarization and statistical analysis. Collection of electronic and physical data from each health facility was the sole responsibility of the primary investigator who was based in, and travelled across Seychelles, during the interval period in order to access reference lists retained by primary physicians and to then access and screen individual patient records and input data into the primary electronic database.

Individuals suitable for qualitative interviewing were selected purposively by primary physicians located within the two largest-serving primary health centres in Victoria, Mahé, in order to capture adults aged ≥ 18 years and those who were most likely to provide in-depth information concerning the impact of chronic rhinosinusitis. Patients meeting the criteria were invited to participate in interviewing by their primary physician and, upon acceptance, a record of contact details was retained for the interviewer to arrange mutually convenient times to conduct the interviews. Patients were contacted in a non-random but consecutive order. Qualitative data was collected using a face-to-face, semi-structured interviewing technique with open-ended and closed questions that focused upon eliciting the physical, psychological and emotional impact of chronic rhinosinusitis upon individuals who had received a clinical diagnosis. A copy of the interview question form is provided in Appendix 1. A sample of eight individuals was initially sought, but recruitment and interviews continued until the data became theoretically saturated, which resulted in a final sample of 11 subjects. All interview data was audio recorded and transcribed verbatim, which was then translated into English using a professional service and then organised and managed on an electronic database to permit thematic analysis using open-coding as defined by Braun and Clarke (2006).

The incidence and prevalence of chronic rhinosinusitis was defined and calculated using formal operational definitions and equations (Spronk et al., 2019). The incidence of chronic rhinosinusitis, as a representation of the frequency of new diagnoses over a specific time period, was calculated using overall and yearly numerators and with various denominators, including incidence rate in person-years and the overall cumulative incidence. The incidence rate was calculated as the number of new cases of chronic rhinosinusitis/number of persons at risk of chronic rhinosinusitis, of which the latter comprised the total population in the Seychelles given that an at-risk cohort has not been previously established or defined. The cumulative incidence was calculated as the number of persons diagnosed with chronic rhinosinusitis over the four-year study

period/the number of persons at risk of chronic rhinosinusitis, which again comprised the total population as formerly noted.

Similarly, the prevalence, as a reflection of the proportion of a defined population affected by chronic rhinosinusitis, was calculated using various numerators and denominators. The point prevalence was calculated as the number of cases of chronic rhinosinusitis at a single time point/the total population at the same time point, whilst the period prevalence was calculated for each study year as the number of cases over each year/the mean total population for the same year. Estimates of the total population size for each interval year were derived from census data provided by the National Bureau of Statistics (2019a). Temporal variations in incidence and prevalence of chronic rhinosinusitis in terms of percentage change were also calculated and represented graphically and statistically with a standard alpha of 0.05 representing the threshold for significant differences between time points. Odds ratios with 95% confidence intervals for the former at-risk groups were calculated using a standard 2x2 table and formula of: (number of exposed cases/number of unexposed cases)/(number of exposed non-cases/number of unexposed non-cases). Finally, the incidence, prevalence and odd ratios were also stratified for age groups and geographic regions within Seychelles. All data was analysed and managed using IBM SPSS Statistics version 25 (IBM United Kingdom Ltd, Hampshire, UK).

Approval for this study was authorised by the local Health and Research Ethics Committee of the Ministry of Health, Seychelles, in May 2019.

Results

(a) Quantitative data

For the defined study period, the total population in Seychelles increased by 4,206 from 93,419 in 2015 to 97,625 in 2019. Over the four-year study interval, a total of 2,857 cases of chronic rhinosinusitis had been documented by physicians in Seychelles, although the number of ascertained cases, through review of case notes by the primary investigator and correlating clinical data with diagnostic criteria, totalled 1,983 persons (38.3% male, 61.7% female), who were included in the final analysis. The baseline characteristics of the study population are summarised in Table 1 below. The mean age of the entire cohort was 28.9 years and the mean duration of chronic rhinosinusitis was eight months. Among adults aged ≥ 18 years, the mean age of those diagnosed with chronic rhinosinusitis was 37.7 years whilst for children aged < 18 years, the mean age was 8.4 years. Most subjects were resident within Mahé, followed by Praslin and La Digue. The proportion of subjects diagnosed with asthma, atopic dermatitis, and other allergic conditions was 23.2%. Among adults, 34% were current smokers, 32% previous smokers and 45% had never smoked. Among current smokers, the percentage of the cohort who

had been diagnosed with chronic rhinosinusitis was 6.80%, which was similar to previous smokers (6.11%) but higher than those who had never smoked (1.89%); see Figure 1 below. Among persons with one or more allergic conditions, 3.82% of the cohort had chronic rhinosinusitis as compared to 2.35% for those without one or more allergic conditions.

For the qualitative analysis, a total of 10 subjects (7 female, 3 male) were interviewed who had a mean age of 45 years and a mean duration of chronic rhinosinusitis of seven months (range 4-10 months). All other baseline characteristics are detailed in Table 2, below. None of these subjects had ever smoked or been diagnosed with any allergic conditions.

Table 1. Baseline characteristics of epidemiological cohort

Demographics/Clinical Characteristics	Time Interval/Statistics (n/%)			
	Year 1	Year 2	Year 3	Year 4
Total	423	456	387	717
Age				
0-4	21 (5.0%)	7 (1.5%)	11 (2.8%)	32 (4.5%)
5-10	112 (26.4%)	123 (24.6%)	111 (28.7%)	176 (24.5%)
11-17	45 (10.6%)	27 (5.9%)	25 (6.5%)	86 (12.0%)
18-30	68 (16.2%)	86 (18.9%)	87 (22.5%)	95 (12.3%)
31-50	89 (21.0%)	96 (21.1%)	79 (20.4%)	171 (23.8%)
50+	88 (20.8%)	117 (25.7%)	74 (19.1%)	157 (21.9%)
Gender				
Male	178 (42.1%)	163 (35.7%)	178 (46.0%)	251 (35.0%)
Female	245 (57.9%)	293 (64.3%)	209 (54.0%)	466 (65.0%)
Residence				
Mahé	387 (91.5%)	289 (63.4%)	303 (78.3%)	569 (79.4%)
Praslin	24 (5.7%)	93 (20.4%)	64 (16.5%)	102 (14.2%)
La Digue	12 (2.8%)	74 (16.2%)	20 (5.2%)	46 (6.4%)

Chronic Rhinosinusitis	Physician Diagnosed	627	663	536	1031
	Case-Ascertained	423	456	387	717
	Mean Duration of Diagnosis (months)	6	9	8	8
Allergic Conditions/History	Asthma	101 (24.2%)	123 (29.0%)	178 (46.2%)	255 (35.7%)
	Hay fever	51 (12.6%)	109 (24.5%)	129 (33.5%)	195 (27.2%)
	Dermatitis	158 (37.3%)	205 (45.8%)	47 (12.1%)	156 (21.8%)
Smoking Status	Current	157 (37.1%)	179 (39.3%)	121 (31.2%)	257 (35.8%)
	Past	111 (26.2%)	163 (35.7%)	98 (25.3%)	198 (27.6%)
	Never	155 (36.6%)	114 (25.0%)	168 (43.4%)	262 (36.5%)

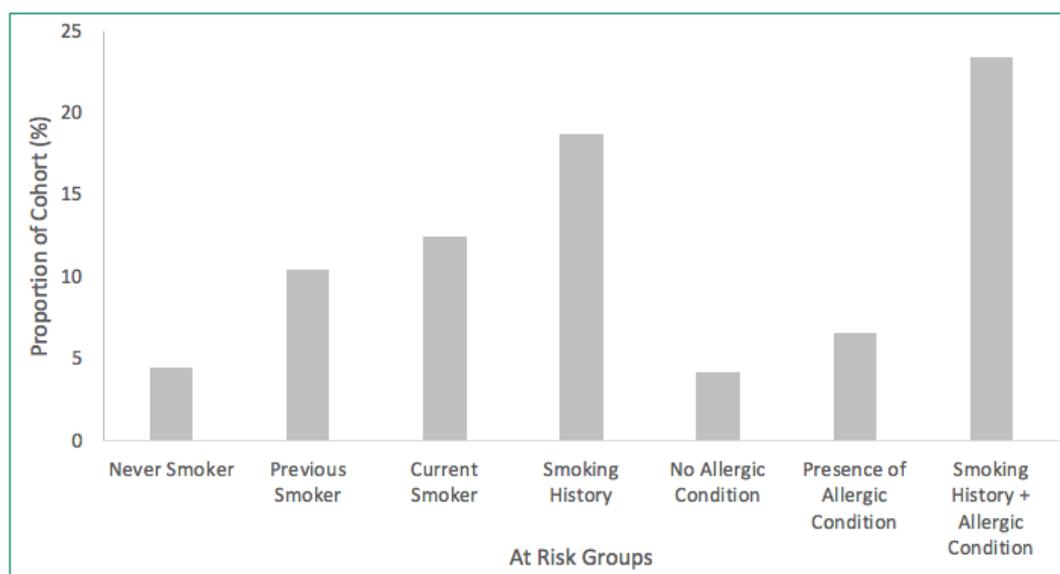


Figure 1. Smoking and allergic history status of subjects with chronic rhinosinusitis

Table 2. Baseline characteristics of qualitative cohort

Demographics/Clinical Characteristics	Statistic (n/%)
Age (mean)	45
Gender Male Female	3 (30%) 7 (70%)
Residence Mahé Praslin La Digue	10 (100%) 0 0
Chronic Rhinosinusitis Physician Diagnosed Case-Ascertained Mean Duration of Diagnosis (months)	10 (100%) 10 (100%) 7
Allergic Conditions/History Asthma Hay fever Dermatitis	0 0 0
Smoking Status Current Past Never	0 0 10 (100%)

The number of new case-ascertained diagnoses of chronic rhinosinusitis over the study interval were 45 during year one, 28 during year two, 19 during year three and 65 during year four; which equated to respective incidence rates of 2.30%, 1.41%, 0.96% and 3.28%. Overall, the incidence remained relatively stable over the four-year study period

with a maximal yearly variance of 46 new diagnoses or 2.32%, see Figure 2 below. The cumulative incidence over the four-year interval for the entire cohort was calculated as 1.97%. For adults aged ≥ 18 years, the annual incidence rates were 1.91%, 1.46%, 1.03% and 3.18% during years one, two, three and four, respectively, and were comparable to children aged < 18 years (year one: 2.45%, year two: 1.37%, year three: 0.94% and year four: 3.35%), see Figure 3 below. The cumulative incidence of chronic rhinosinusitis in adults was 1.90%, which was 0.38% lower than children who observed a cumulative incidence of 2.28%. The mean incidence of chronic rhinosinusitis for adult and paediatric age groups defined in categories of 0-4, 5-10, 11-17, 18-30, 31-50 and 50+ years ranged between 0.4% and 3.31% and was highest for children aged 5-10 years (3.31%) and adults aged 31-50 years (2.96%), see Figure 4 below.

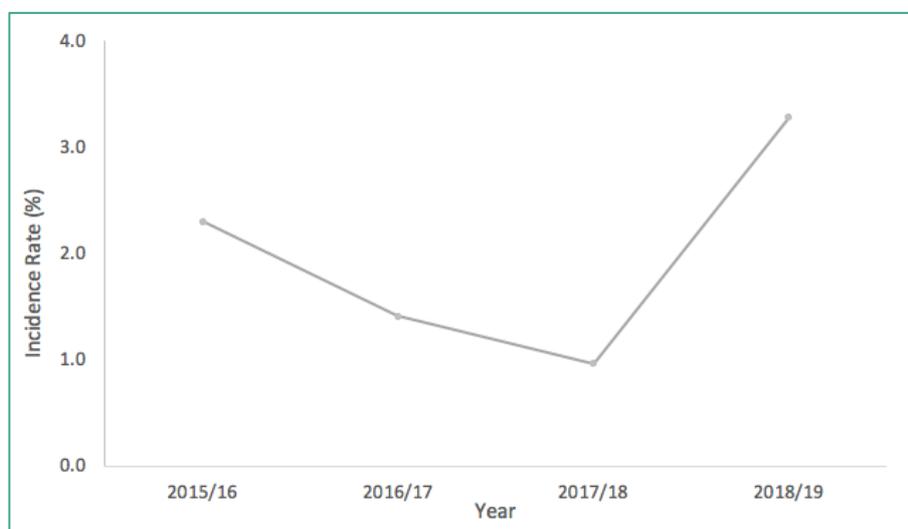


Figure 2. Annual incidence of chronic rhinosinusitis during 2015-2019



Figure 3. Annual incidence of chronic rhinosinusitis in adults and children during 2015-2019

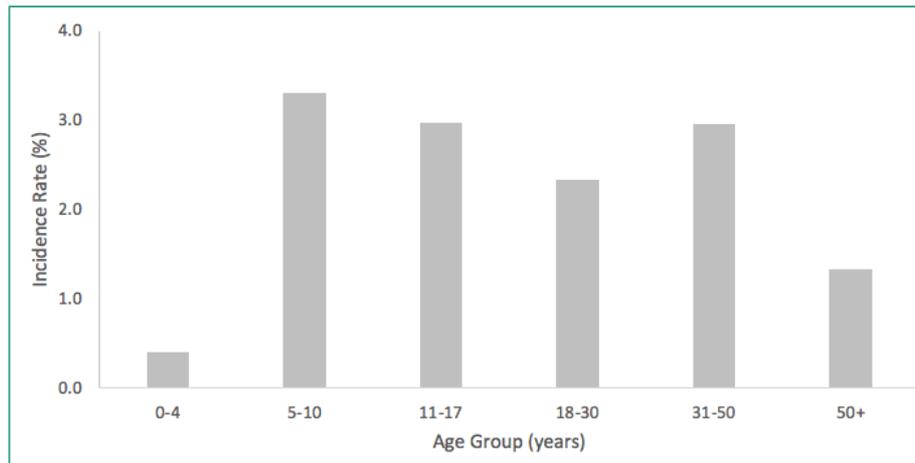


Figure 4. Mean incidence of chronic rhinosinusitis by age group

For the entire cohort, the period prevalence rates for year one, two, three and four were calculated as 4.62%, 5.12%, 5.35% and 7.54%, respectively (Figure 6 below) and the point prevalence at the most recent time-point in March 2019 was 7.59%. For adults aged ≥ 18 years, the period prevalence rates were 4.56%, 5.01%, 5.20% and 6.89% during years one, two, three and four, respectively. For children aged < 18 years, the period prevalence rates were 4.78%, 5.23%, 5.75% and 8.21% during years one, two, three and four, respectively (Figure 7 below). The point prevalence at the most recent time-point in March 2019 was 6.92% for adults and 8.34% for children. The point prevalence of chronic rhinosinusitis by age group was greatest among children aged 5-10 years (8.26%) and adults aged 31-50 years (6.84%), see Figure 8 below.

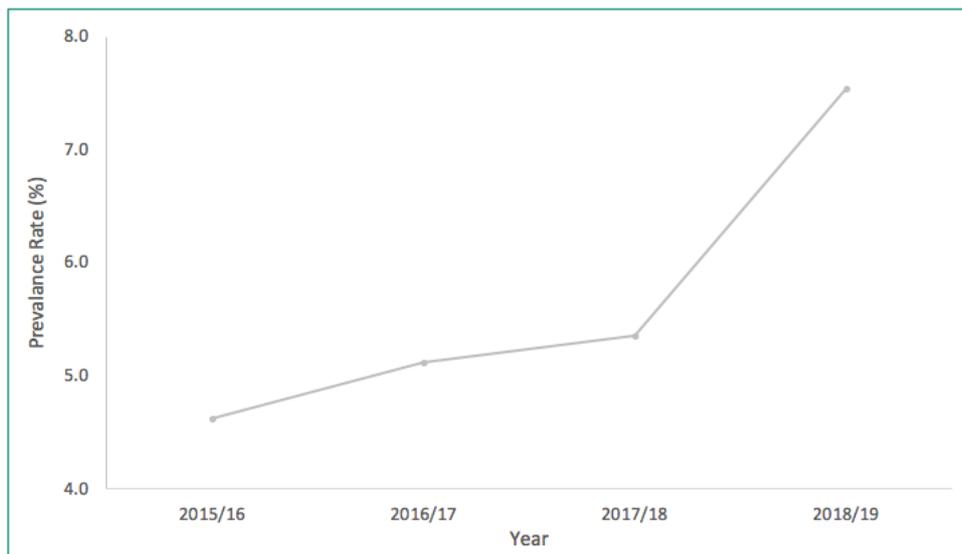


Figure 6. Prevalence of chronic rhinosinusitis during 2015-2019

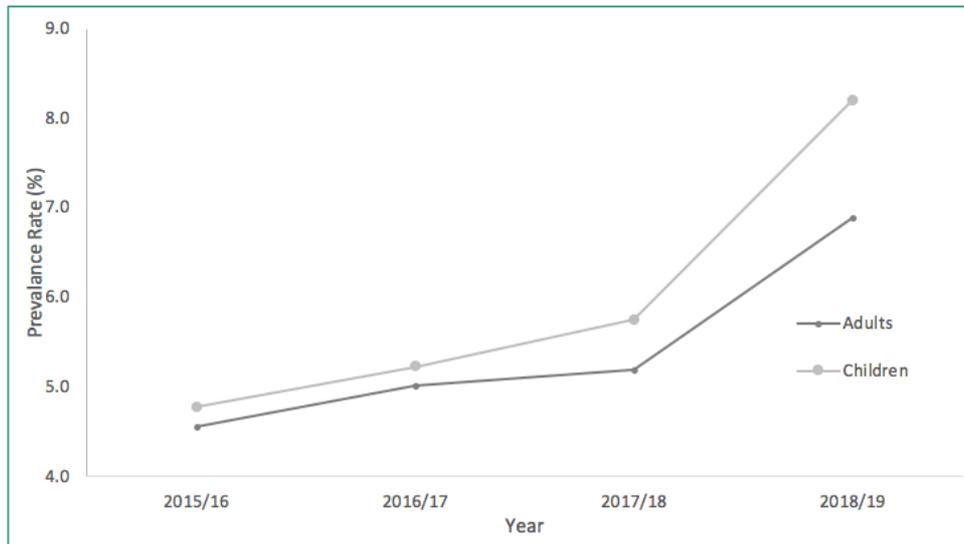


Figure 7. Prevalence of chronic rhinosinusitis in adults and children during 2015-2019.

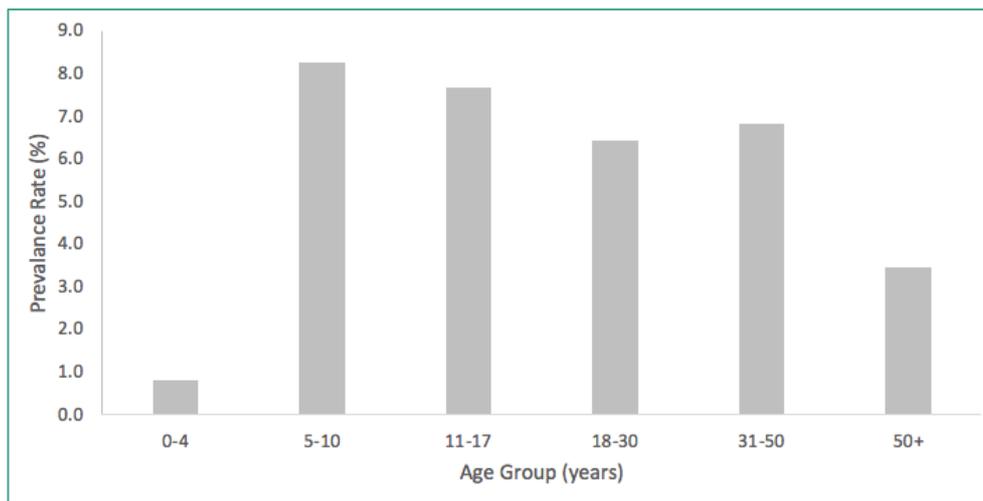


Figure 8. Prevalence of chronic rhinosinusitis by age group

The odds ratios (OR) for the former at-risk groups were calculated to quantify the risk of chronic rhinosinusitis during the study interval period. For smoking status, the risk of chronic rhinosinusitis was greatest for current smokers (OR 1.39; 95% CI 1.11, 1.74), followed by previous smokers (OR 1.23; 95% CI 1.03, 1.56) and never smokers (OR 1.10; 95% CI 0.75, 1.24), whilst those with one or more diagnosed allergic conditions observed an OR of 1.18 (95% CI 1.02, 1.37). The risk of chronic rhinosinusitis was greatest among persons with a smoking history and diagnosed allergic condition (OR 1.41; 95% CI 1.22, 1.85). One-way ANOVA revealed that the association between all risk factors and chronic rhinosinusitis were statistically significant (all $p < 0.001$).

(b) Qualitative interview data

Thematic analysis of the qualitative interview data revealed consistencies that generated two main themes of: impact upon self, and impact upon others. These themes are presented below along with a select number of direct quotations from participating subjects for contextual support.

Theme 1: Impact upon self

The responses of subjects revealed that chronic rhinosinusitis markedly and negatively impacted upon their perceptions of general health status, emotional/psychological wellbeing and quality of life despite the majority of participants recognizing that the symptoms of chronic rhinosinusitis were relatively minor when compared to the manifestations of other diseases and conditions. For example, a number of subjects diagnosed with chronic rhinosinusitis and complaining of persistent nasal blockage and facial discomfort reported that this combination of symptoms was highly unpleasant and the lack of effective treatments to ameliorate these problems led to progressive increases in frustration and distress over time, which altered and shaped perceptions of general health status to one that was rated by most subjects as poor. This perception was even despite chronic rhinosinusitis being many subjects first and only diagnosed medical disease, although some participants with one or more pre-existing comorbidities perceived the impact of rhinosinusitis to be an additional burden and merely perpetuated their ability to recover from ill health and achieve their pre-co-morbid status. In contrast, two individuals reported a satisfactory health status but this was attributed to the efficacy of analgesic interventions, which had improved the intensity of facial discomfort/pain and this appeared to lower the degree of emotional and psychological stress experienced and attenuate the cumulative effect of this stress upon the development of more serious psychological and psychiatric morbidity.

When I was diagnosed... I thought this was it... a downhill slope to poor health and death. [S1]

The blocked and runny nose and the pain around my face was awful and this often made me feel as though I had a terminal illness. [S2]

It [diagnosis] was another medical problem... one of many... my health was taking a big hit and my health seemed to be getting as poor as those who were suffering from cancer and stroke. [S7]

Indeed, three subjects reported having experienced symptoms that met the criteria for depression or had been diagnosed and treated for depression by a primary physician. One subject noted that she became emotionally overwhelmed only after a short period of attempts to endure and tolerate the protracted discomfort associated with chronic rhinosinusitis, which in turn, resulted in her experiencing feelings of hopelessness and

sadness that deteriorated into a mentally ill state comprising low energy, sleeplessness and a lack of desire to engage with daily occupations and life. Indeed, other subjects recognized that the problem impacted upon their daily lives with the persistent nature of symptoms acting as a constant unpleasant issue during the day, which affected their ability, desire and performance with both leisure- and work-related tasks. For example, one participant stated that chronic rhinosinusitis often impaired their ability and desire to communicate with clients and colleagues and even when symptoms could be tolerated or were minimal in intensity, the residual discomfort acted as an inhibitor of memory recall and cognitive executive function, which affected their work performance and, specifically, tasks requiring forward planning. The unpleasant nature of symptoms even affected individual's ability to enjoy and partake in leisure activities, hobbies and social events, which left many people feeling as though they could never escape from the disease and, as a result, this was reported to be one of the greatest psychological stressors such people had experienced throughout their lives. The former subject even reported that she had suffered several episodes of severe depressive disorder with psychosis as a result of various stressors, but with chronic rhinosinusitis being the primary source exacerbating all forms of stress. This participant had even received inpatient compulsory admission and treatment for severe depression as a result of self-harm and suicidal ideation, although she admitted to having never made any plans or active attempts upon her life. On additional exploration of the psychiatric impact of chronic rhinosinusitis with the subject being largely and voluntarily forthcoming, it became apparent that the manifestations of the diagnosis were so burdensome that the only escape and relief from pain and discomfort was to harm herself as a noxious distraction or to take her own life, although her grandchild was a protective factor that has, thus far, prevented the latter.

Things became so difficult after getting it [rhinosinusitis]... I became a depressed person... for the first time in my life... I felt trapped and unable to pull myself out of feeling sad, it was as though I was on a one-way road to more problems. [S8]

The depressive stage... it affected everything, sleeping, eating, doing jobs, going out and socializing... soon life became unbearable. [S7]

The symptoms were the main problem, the pain was severe, always there and the only relief I found was cutting myself... I once thought about taking my life but I have a grandchild and she is my only light. [S10]

The psychological and psychiatric sequelae of chronic rhinosinusitis were reported to be the principal problems impairing perceived quality of life. For most subjects, quality of life was defined as having an ability to enjoy life and experience happiness and contentedness, although both of these experiences had been diminished or were increasingly difficult to experience as a result of chronic rhinosinusitis. Subjects stated that they were still able to feel a sense of happiness and experience enjoyment in life, but that the symptoms of chronic rhinosinusitis had reduced the maximal positive impact

that these emotions could have upon their long-term health and wellbeing. In this regard, it appeared that the protectiveness of these emotional experiences had become less effective over time with chronic rhinosinusitis, and that subjects could not retain enough self-reserve and resilience in order to engage with self-care tasks and activities that could otherwise enhance the impactfulness of positive emotional states. This was particularly evident in subjects who had sought professional advice and support to assist them in becoming more resilient and able to overcome adversity, such as through counselling and cognitive behavioural therapy, which were reported to be ineffective and were simply an additional failure that heightened individuals perceived levels of hopelessness and apathy. Notably, a number of subjects had completely abandoned conventional western medical treatment approaches and, instead, sought help from ancient Seychellois practices of witchcraft and sorcery as a last resort to attain symptomatic relief even despite having prior beliefs that these practices were bogus and nonsensical.

The problem dampened my emotional senses but just the positive ones... I used to laugh and enjoy life but no more... I have changed... my personality has changed. [S4]

I initially tried to use my inner strength to help me cope but over time it was difficult to keep going... even talking treatments recommended by the doctor were not effective... nothing seemed to be helpful. [S9]

The problem made me feel so hopeless but before I lost all hope I tried traditional Seychellois practices... you know witchcraft and magic and wizardry... I did not believe in these before but felt I had no choice. [S6]

Another concerning problem reported by two subjects in the interviews relating to the theme of impact upon self, was that chronic rhinosinusitis was perceived as being as burdensome as other and more serious health problems, including cancer and diabetes. These participants had lived with chronic rhinosinusitis for protracted durations of time and this appeared to have altered their cognitions and objectivity concerning health and disease, with them relating their non-mortality lowering condition and lives to those of previously close relatives who had died from life-limiting illnesses. However, these reports demonstrate that quality of life and life content are highly subjective perceptions and can never be fully understood by individuals other than themselves – an observation that one subject was able to clearly vocalise. Notably, this subject had even made advanced planning decisions regarding their future care, albeit being relatively young, and these were erroneously centred around expectations concerning premature mortality, which led to advanced refusals of overly invasive medical care and a desired preferred place of death as being their home environment.

The problem has been with me for so long... it has affected me as it did with my father's cancer. [S6]

Medicine does not recognize the effect of rhinosinusitis upon my life, the doctor does not but I believe I will die early. [S10]

I have made plans for the future already, dying at home and I don't want resuscitation. [S10]

Theme 2: Impact upon others

The impact of chronic rhinosinusitis was consistently reported to affect most subjects' social and personal relationships. In the social setting, some subjects stated that peers, colleagues, and even their closest friends and relatives adopted more distant interactions with them, due to erroneous misconceptions and fears that the symptoms of chronic rhinosinusitis were a transmissible infectious disease. One participant reported that although they had explained their diagnosis to one of their good friends and emphasized that it was a benign and non-infectious problem, the number of communications and in-person interactions had declined over time and even after continual efforts to maintain the relationship through phone calls and messaging, contact eventually ceased and the friendship ended. For many subjects, the loss of social relations was one of the most significant stressors as this made them feel angry, frustrated and worthless of self, which rapidly evolved into withdrawal and active attempts to isolate themselves from the external environment and human interaction entirely. Indeed, most subjects recognized that this event was a critical point in their course of mental ill health with its onset triggering a transition of feeling in control to out of control of their feelings, emotions and thoughts. This problem was found to have a number of exacerbating factors. Firstly, some subjects reported that their primary physician was readily able to diagnose chronic rhinosinusitis but despite having the appropriate education, training and experience, they did not offer support and tended to communicate that the problem was something that they had to simply cope and live with, and this exacerbated feelings of hopelessness. Secondly, subjects with chronic rhinosinusitis even failed to receive emotional support and empathy from their friends and families, with such individuals having compared chronic rhinosinusitis to a common cold, which markedly undermined the chronic and debilitating nature of the disease and conveyed that it was something every human had experienced and could overcome. Moreover, individuals known to affected subjects had trivialized chronic rhinosinusitis to such an extent that it had become a central source of humour within their network and a means to passively dismiss talking about the disease without identifying and seeking opportunities to understand the impact of the problem, which left most subjects feeling socially excluded despite retaining some level of inclusion. In turn, this complex social issue left participants feeling as though they had to induce humour about the problem upon themselves, in order to retain status within their social circles, whilst feeling markedly stigmatized and burdened by the problem.

It was hard for others to understand... they thought it was just the flu and attempts to explain that it was different did not work. [S3]

My friends even thought that it was a highly infectious disease... and became distant. [S2]

My way of coping and to fit in was to use the problem as a source of humour but inside I was really struggling... I felt isolated... [S7]

In contrast, the spouses and intimate partners of subjects were more empathic and understanding of their chronic rhinosinusitis, but other participants reported that the problem had significantly affected their relationships, and for one subject the disease became such a focal and irretractable issue that it affected all aspects of their relationship and ultimately induced divorce proceedings. In this case, the symptoms of chronic rhinosinusitis were reported to be so troublesome that it not only impaired their ability to engage in interactions with their spouse but it had also affected their child's development and behaviour, which was perceived to be a result of absenteeism from parenting and a reliance upon other members of the family that induced confusion and conflict. Other subjects recognized that the nature of chronic rhinosinusitis affected the intimate component of their relationships as it impeded the ability to convey love and enjoyment of one another, which had a number of negative emotional effects and repercussions that often resulted in relationship breakdowns or stimulated the emergence of other issues that simply increased the degree of stress experienced by both parties. Whilst most subjects reported that they could contain the negative symptomatic impact of chronic rhinosinusitis and prevent the problem from affecting their performance at work, the intensity of emotional stress experienced as a result of relationship issues and difficulties appeared to rapidly overwhelm their coping capacity, leaving most participants unable to complete work tasks. Notably, the reductions in productivity and concentration at work were almost always noticeable and led to either formal or informal disciplinary hearings and this induced fear concerning the threat of losing their job/career and the subsequent financial strains whilst looking for alternative employment. Financial anxiety was a clear source of stress for many subjects who reported that their lives depended upon their job/career with their children, housing and other dependents relying upon a stable source of monetary income. Some subjects identified that their occupation was their family's main income source and that communicating this anxiety with their spouses placed additional stress upon their relationship, which in turn, worsened symptoms of chronic rhinosinusitis, leading to a continuous worsening cycle of debilitating symptoms and stress.

I now recognize that it was my fault [marriage breakdown] for not seeking help to manage my disease but I still blame the disease and western medicine for not having any useful treatments. [S9]

The symptoms were so intense that it affected all aspects of my relationship... the behaviour of our child changed... she became emotionally labile and detached... and showing affection to my wife became challenging and this obstructed the love we had developed over the years. [S7]

Sometimes on bad days the symptoms were always there and medication failed to work... this stopped me doing my job and colleagues began to notice but they could not sympathize and seemed to judge me... even to a point where they made me feel as though I was making it up. [S5]

Later on... work became such a problem that I feared for loss and the future impact upon my family... how was I going to support them financially. [S5]

The negative effects of chronic rhinosinusitis also extended to affect subjects' interactions and relationships with their children, which often induced feelings of sadness and disappointment as these individuals perceived that their child's development and success in later life would be compromised by their health problem. These participants reported that their children of pre- adolescent and adolescent ages were approaching critical times in their life with pubertal development and imminent transitioning into adulthood and that the debilitating nature of chronic rhinosinusitis symptoms obstructed the ability of subjects to support and influence their lives during these times. Subjects thought that this was going to alter the course of their future lives in regard to occupational, social and relational aspects, but to one of lower desirability and content, than if their lives were to have received greater influence through frequent interactions and communication about life issues. More specifically, participants reported that they were unable to give advice to their children and offer insight into decision making and problem solving, which were perceived as fundamental factors influencing the ability to excel and cope with various life stressors. Notably, one participant recognized that their child had received ongoing advice regarding life issues from their healthy partner (wife/mother), their children's development was perceived as being negative given that their child was perceived to have been brought up at a crucial time in a single-parent-like situation.

One of the most sad things was... well... you know, I was unable to help my child through difficult problems. [S10]

I felt like a failure as a parent, their development was important and I could not guide them. [S9]

It was as though I was not there, my partner helped but single-parenting is not the best path to having and leading good lives for children. [S9]

One of the most alarming reports of this qualitative interview component was reported by a male subject who, along with their spouse, had been the principal care-givers for their child who had congenital cognitive deficits and physical disability; but the additional strain and dependence placed upon his partner following the diagnosis of chronic rhinosinusitis had clear negative impacts upon all parties. Firstly, his partner encountered a progressive increase in dependent demand and related stress that, over

time, became reflected in outbursts of frustration and anger regarding her life position. Notably, the child appeared to sense the negativity and, as a result of this and the disruption to their usual routine, their physical, behavioural, and cognitive status declined and became increasingly erratic, which became an additional source of stress for both the subject and his partner. Secondly, this situation became exacerbated by the subject's increased care needs related to chronic rhinosinusitis within the home environment, which not only contributed to the stress of his partner but also led to her developing intermittent mild illnesses that affected her ability to care for her loved ones. This family dynamic became rapidly dysfunctional and increasingly complex where stability was compromised by conflict, tension and intense emotions. This appeared to blunt and impair reasoning, negotiation and decision making between family members, which encouraged the subjects to suppress and internalize emotions and thoughts and, in turn, this markedly enhanced their risk of psychological and psychiatric morbidity. The subject and her partner also failed to seek support from their relatives despite having a large family network, reporting that it was their problem to solve and overcome in isolation although finding it increasingly challenging to achieve this goal.

Diagnosis was the start of all the problems, it affected me, my wife and our disabled child.
[S2]

She [wife] has been the main carer for our child with me working and then my sinus problem.... she could no longer cope... there was stress, anger and volatility... it became a recipe for disaster. [S2]

Discussion

In response to the global burden of chronic rhinosinusitis and local anecdotes of its growing prevalence and impact within Seychelles, this research aimed to delineate for the first time the epidemiology of chronic rhinosinusitis across the nation's most populous islands, and to explore the impact of the disease upon individuals' lives in order to generate evidence that could be used to inform clinical guidelines and to guide more appropriate and equality-promoting policy decision making. In turn, it was hoped that the findings and their influence upon practice and policy change would improve outcomes and attenuate the burden of chronic rhinosinusitis in the long term. Utilizing a mixed-methods approach, the prospective epidemiological component found that 1,983 persons were clinically diagnosed and ascertained to have chronic rhinosinusitis over the four-year interval between 2015 and 2019, with the incidence rate varying between 1.0-3.3% and the prevalence demonstrating a progressive temporal increase from 4.6% in 2015 to 7.5% in 2019. The mean incidence and prevalence rates were found to be highest among the paediatric age group of 5-10-year-olds (3.3% and 8.3%) and the adult age group of 31-50-year-olds (3.0% and 6.9%). Both smoking history and co-existing allergic conditions were found to be associated with a higher incidence and prevalence of

chronic rhinosinusitis than their contrasting counterparts and, in combination, these risk factors were associated with an incidence of 7.4% and a prevalence of 23.4%. Indeed, smoking and allergic condition history was associated with a 41% increased risk of chronic rhinosinusitis with the respective risks in isolation being 39% and 18%.

This is the first study to elicit the epidemiology of chronic rhinosinusitis within Seychelles and, thus, the findings can only be compared with epidemiological data reported among other nations. In one study, Dietz de Loos et al. (2019) found that the prevalence of chronic rhinosinusitis in the Netherlands, that was ascertained using clinical, radiological and endoscopic criteria, varied between 3.0-6.4% depending upon radiological cut-off scores using the Lund-Mackay system, which is similar to this study. Among other epidemiological cohorts, the prevalence of chronic rhinosinusitis has been markedly similar and averaging around 5-10% among both western and non-western countries (Gilani and Shin, 2017; Beule, 2015; Bachert et al., 2014). Although most epidemiological studies into chronic rhinosinusitis have been able to report upon the incidence and prevalence of subtypes, including nasal polyp positive and nasal polyp negative rhinosinusitis, this data was not possible to extrapolate in this study given the lack of availability and utility of endoscopic/radiological equipment to confirm the diagnosis in Seychelles. The reason for temporal increases in the prevalence of chronic rhinosinusitis identified may be attributed to the rising and emerging epidemic of obesity in Seychelles with evidence having previously suggested that obesity is a risk factor for otorhinological disease, although the association has not been consistently confirmed statistically (Sidell, Shapiro and Bhattacharyya, 2013). For example, a large cross-sectional analysis of the United States Medical Expenditure Panel Survey showed that the risk of chronic rhinosinusitis in obese persons was significantly greater (adjusted OR: 1.31; 95% CI 1.18, 1.45, $p < 0.001$), than compared to persons of a healthy body mass index. In addition, the significant association between obesity and chronic rhinosinusitis increased with progressive increases in body mass index, suggesting that obesity is contributing to the growing burden of rhinosinusitis, among other sinonasal disorders (Bhattacharyya, 2013). Indeed, the prevalence of simple overweight and obesity in Seychelles has increased markedly in recent times by 33% in men and 17% in women over 15 years leading up to 2004 and, concerningly, this trend has continued to the present day where the mean annual change in obesity has exceeded 4% for the last five years (Bovet et al., 2008; World Data Atlas, 2019).

Notably, several studies have previously demonstrated associations between the severity of allergic conditions, such as asthma, and obesity, and its relationship with rhinosinusitis has been attributed to the subclinical hyperinflammatory state of obesity and amelioration of immune system function (Shore, 2010; Ali et al., 2018; Hersoug and Linneberg, 2007). Evidence has also identified that persons with the more severe forms of chronic rhinosinusitis, and those with refractory symptoms with poor responses to therapy, often have a co-existing dyad of allergic rhinitis and asthma, suggesting that there is a common underlying inflammatory mechanism of disease and predisposition to

developing rhinosinusitis over time (Rosati and Peters, 2016). Whilst the prevalence of chronic rhinosinusitis was heightened among those with co-existing allergic conditions in this study, tobacco smoking also contributed to the overall burden and, indeed, both passive and active smoking have been pathophysiologically associated with chronic rhinosinusitis through its direct injurious effect upon the innate immune system (Reh, Higgins and Smith, 2012). This association has been supported among various other studies and are cited here for the reader's reference (Shore, 2010; Ali et al., 2018; Hersoug and Linneberg, 2007; Tomassen et al., 2011; Gordts, Clement and Buisseret, 1996).

In this study, there were also age-related variances in the incidence and prevalence of chronic rhinosinusitis with the highest rates occurring in children, and this is likely to be attributed to previously-documented associations with gastroesophageal reflux and otitis media, which are not as common in adults (Mahdavinia and Grammer, 2013). Indeed, Gilani and Shin (2017) showed that chronic rhinosinusitis was significantly more likely in children aged 5-10 years and 11-15 years, than those aged <5 years, which is congruent with the peak incidence and prevalence of the disease in this study's paediatric cohort. Moreover, Sedaghat et al. (2013) suggested that chronic rhinosinusitis can naturally progress from allergic rhinitis, but that a significant proportion of these individuals have variances in sinonasal anatomy that increase the rate of progression some 68-fold, although, due to the lack of endoscopic investigative equipment, this observation could not be supported in this study. Whilst variances in the incidence and prevalence of chronic rhinosinusitis may also be attributed to a multitude of other factors, this would require additional exploration in future research. Indeed, the qualitative findings of this study could act as a potent stimulus to drive further research into chronic rhinosinusitis in Seychelles, particularly given that the experiences of affected subjects were consistently reported to induce emotional, relational and occupational stress and, in turn, promoted the development of psychological and psychiatric morbidity. These consequences were not only found to affect almost all aspects of individuals' lives and reduce perceived quality of life, but also confirmed that chronic rhinosinusitis can have societal-level implications as a result of losses in productivity and community engagement, which could be obstructing the developmental status of Seychelles as a collective nation.

Comparison of the qualitative findings of this study with wider literature indicate that chronic rhinosinusitis is a highly burdensome disease and one that has been largely under-estimated, particularly as other leading health issues often take precedence for policy decision making (Rudmik and Smith, 2011; Nyaiteera et al., 2018; Tan et al., 2013). In the study by Nyaiteera et al. (2018), the authors conducted a cross-sectional analysis of 126 adults diagnosed with chronic rhinosinusitis to assess quality of life using the validated Sinonasal Outcome Test 22 instrument, which includes measures of physical function and psychological wellbeing. Although the response rate was relatively poor (39%), a significantly greater number of patients with rhinosinusitis reported scores

that were congruent with a poor quality of life, than compared to the number of control subjects also reporting poor quality of life scores (88% v. 20%, $p < 0.01$). The authors found that poor quality of life scores were mostly associated with moderate to severe nasal symptoms, whilst high educational attainment and a desirable socioeconomic status were protective of life quality. However, due to the qualitative approach adopted in this study, the exacerbating and protective influences of perceived quality of life among Seychellois people could not be ascertained. Despite this, other authors have found that females with chronic rhinosinusitis tend to observe poorer quality of life than their male counterparts (FERENCE et al., 2015), and, indeed, this was reflected in this study with the qualitative component comprising a predominance of female participants (70%).

The principal strengths of this study were the prospective epidemiological design and the subsequent capture and analysis of a large representative sample of the Seychellois population. Given that the cohort originated from the most populous islands of Seychelles, the findings of this study could be generalized to less populous areas, particularly given that the collection of qualitative data reached the theoretical saturation point. Moreover, the study adopted a mixed-methods design to help address two important knowledge gaps which in combination have yielded sufficient evidence to inform and make recommendations to current clinical practice, chronic rhinosinusitis guidelines, and policy decision making. The limitations of this study were varied but are not thought to have significantly affected the internal validity of the results. Firstly, the identification of incident cases of chronic rhinosinusitis relied upon the vigilance of physicians across the various primary health centres to document clear and accurate records for the investigator to review and ascertain at a later time point, which is inherently subject to error and may have resulted in case under-detection. Secondly, whilst the case ascertainment process and criteria was appropriate and utilized formal European Position Paper of Rhinosinusitis (EPOS) guidelines (Fokkens et al., 2012), diagnosis of chronic rhinosinusitis could only be ascertained clinically, given that health centres have very restricted access to radiological and endoscopic investigations for patients with upper respiratory pathology. This could have resulted in either under- or over-ascertainment of diagnosis, with the latter being particularly relevant given the possibility of contamination with differential diagnoses that can mimic chronic rhinosinusitis. This resource issue also prevented the ability to derive the epidemiology of the subtypes of chronic rhinosinusitis, which may limit the extent and specificity of changes to local guidelines. Indeed, evidence has also shown that reliance upon symptoms alone to ascertain a diagnosis of chronic rhinosinusitis is adequately sensitive but poorly specific, suggesting that this study could have included a proportion of patients with a false diagnosis of the disease (Fokkens et al., 2012). The study was unable to collect data pertaining to subjects' responses to chronic rhinosinusitis therapy that could have helped to improve the reliability of case ascertainment, although this should be a focus for future research where access to objective diagnostic testing equipment is restricted. Thirdly, this study explored the contribution of the risk factors of smoking and

allergic comorbidities upon the incidence and prevalence of chronic rhinosinusitis, but did not collect additional data that may have accounted for some of the variance in the reported epidemiology, such as ethnicity, socioeconomic status and body mass index. Finally, the credibility of the qualitative component of this study was enhanced through data saturation but it was not possible to utilize other techniques, such as respondent validation or triangulation, to validate the findings further.

In conclusion, it is clear that chronic rhinosinusitis is a frequent and burdensome disease affecting both children and adults and wider societies and communities within Seychelles. As suggested by the recent literature, the burden of chronic rhinosinusitis appears to have been markedly under-estimated, but now this novel evidence can be used to attenuate the burden being observed and improve outcomes for affected individuals by stimulating changes to current guidelines, and by triggering greater allocation of funds and resources at a policy level. It is clear that there are multiple methodological challenges to conducting high-quality chronic rhinosinusitis research in Seychelles with the most notable issue being case ascertainment. However, as deriving accurate diagnoses of chronic rhinosinusitis can also be problematic in advanced health settings, it is imperative that this paradigm remains an ongoing research priority, if understanding of the burden and extent of the disease is to be clarified both locally and internationally.

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Appendices

Appendix 1. Semi-structured interview questions

- Tell me about your diagnosis of chronic rhinosinusitis?
 - What was your experience like?
- What is your understanding of chronic rhinosinusitis?
 - Who explained this to you?
- How has chronic rhinosinusitis affected you as an individual?
 - Why was this the case?
 - Why do you feel that way?
- What has been most troublesome about chronic rhinosinusitis?
 - Why was this?
- How has chronic rhinosinusitis affected individuals around you?
 - Family?
 - Friends?
 - Peers/colleagues?
- How has chronic rhinosinusitis affected your quality of life?
 - Why?
- Has chronic rhinosinusitis affected you emotionally and psychologically?
 - In what way?
- Have the psychological effects affected you even more?
 - Psychiatric manifestations?
- How has this affected your occupation?
 - Why?
- How has chronic rhinosinusitis affected your social relationships?
 - Why was this the case?
- How has chronic rhinosinusitis affected your personal intimate relationships?
 - Why was this the case?
- Are there any other concerns or issues you would like to tell me about regarding your diagnosis of chronic rhinosinusitis?