INFERENTIAL ANALYSIS OF BIG DATA IN REAL-TIME: ONE GIANT LEAP FOR SPATIOTEMPORAL DIGITAL EPIDEMIOLOGY IN DENTISTRY

AHMED AL-IMAM

CERVO Brain Research Centre, Faculty of Medicine, University of Laval, Canada;
Department of Anatomy and Cellular Biology, College of Medicine, University of Baghdad, Iraq;
IBM-Certified Specialist: SPSS Statistics;
Microsoft Excel-Certified Data Analyst

SUMMARY
Epidemiological sciences have been evolving at an exponential rate paralleled only by the comparable growth within the discipline of data science. Digital epidemiological studies are playing a vital role in medical science analytics for the past few decades. To date, there are no published attempts at deploying the use of real-time analytics in connection with the disciplines of dentistry. We implemented a real-time statistical analysis in connection with topics in Dental Anatomy and Dental Pathology represented by the maxillary sinus, posterior maxillary teeth, related oral pathology. The purpose is to infer the digital epidemiology based on a continuous stream of raw data retrieved from Google Trends database. Statistical analysis was carried out via Microsoft Excel 2016 and SPSS version 24. Google Trends database was used to retrieve data for digital epidemiology. Real-time analysis and the statistical inference were based on encoding a programming script using Python high-level programming language. A systematic review of the literature was carried out via PubMed-NCBI, the Cochrane Library, and Elsevier databases. The comprehensive analysis of databases of the literature, based on specific keywords search, yielded 491813 published studies. These were distributed as 488,884 (PubMed-NCBI), 1611 (the Cochrane Library), and 1318 (Elsevier). However, there was no single study attempting real-time analytics.
Nevertheless, we succeeded in achieving an automated real-time stream of data accompanied by a statistical inference based on data extrapolated from Google Trends. Real-time analytics are of considerable impact when implemented in biological and life sciences as they will tremendously reduce the required resources for research. Predictive analytics, based on artificial neural networks and machine learning algorithms, can be the next step to be deployed in continuation of the real-time systems to prognosticate changes in the temporal trends and the digital epidemiology of phenomena of interest.

Key words: evidence-based dentistry, public health dentistry, Google Trends, real-time analytics, predictive analytics.

Introduction

Digital epidemiology is an emerging discipline of public health and epidemiological sciences, and it has been evolving rapidly over the past few decades (1, 2). Al-Imam (2017), in his dissertation, pinpointed the absolute necessity to innovate an automated information technology system for data collection and statistical analysis in real-time for the advancement of digital epidemiological studies (3). It can be implemented based on data from online resources of the surface web including trends databases, online drug fora and blogs, and social communication media (3, 4). Google Trends database perfectly fits this

purpose as it contains an automated and up-to-date collection of data based on queries of users of the web from all over the world, including millions if not billions of users (2, 5). Epidemiologist never attempted to carry out real-time or predictive analytics within the context of digital epidemiology and in connection with the discipline of dentistry (6-8). In this study, we will explore this concept via the integrative use of Python programme language, statistical packages, and spreadsheet templates in an aim to demonstrate a prototype for real-time analytic of data retrieved from Google Trends.

The primary objective of this study is to demonstrate a prototype of real-time analysis and to infer data on the digital epidemiology in connection with topics that are related to the maxillary sinus and the Schneiderian membrane, posterior maxillary teeth, and related oral pathologies including periapical abscess formation, periodontal pathologies, and complicated dental implants. Real-time analytics are of considerable impact when implemented in biological and life sciences as they will tremendously reduce the required resources for research. On the other hand, predictive analytics based on artificial neural networks and machine learning algorithms, can be the next step to be deployed in continuation of the real-time systems to prognosticate changes in the temporal trends and the digital epidemiology of phenomena of interest in dentistry, medicine, as well as other subdisciplines of biological and life sciences.

The paranasal sinuses are of prime importance for the region of the head (9, 10). Leonardo da Vinci (1452-1519) made the very first illustration of the maxillary sinus as well as other paranasal sinuses (11, 12). Following a maxillary molar tooth extraction, the treatment modalities routinely involve dental prostheses. However, the central fossa of the candidate implant site may require bone grafting techniques to carry out a satisfactory surgery outcome at the prospective implantation site (13). Oberli et al. analyzed a series of one hundred thirteen periapical radiographs of maxillary premolars and molars with periapical radiolucency indicating chronic apical periodontitis. The cohort was evaluated for the occurrence of maxillary sinus perforations and postoperative complications. Perforation of the Schneiderian membrane occurred in 9.6% of the cases, while membrane exposure without rupture existed in 12%. The distance between the apex of the periapical lesion and the sinus floor did not serve as a predictor of a potential sinus membrane rupture (14). In 2013, Dagassan-Berndt et al. measured the thickness of the Schneiderian membrane via dental Cone-Beam Computed Tomography (CBCT). It was significantly higher in the dentate group compared to the edentulous group in connection with the position of the first and second molar. Further, in the dentate group, clinical signs of periodontal destruction were not associated with Schneiderian membrane thickness (15).

Materials and methods

The Authors have conducted the study by the Declaration of Helsinki, and the Ethics Committee (Institute Review Board) of the College of Medicine at the University of Baghdad (Project Identification Code: IRB7-202017). An analysis of the existing body of literature was conducted systematically from the 1st to the 15th of August 2018 via medical and paramedical databases including NCBI-PubMed, the Cochrane Library, and Elsevier. The unpublished grey literature was also consulted for data of interest. The concept of real-time and predictive analytics was never explored as confirmed via the systematic review of medical and paramedical literature (Table 1A). Further, key words of different themes were utilized in the process of examining the databases of published research in connection with the maxillary sinus anatomy and related pathologies (Table

Table 1A - Investigation of databases of literature: the topic of "Real-time" analysis.

		Number of Hits per Database			
Theme of key words	Key words	PubMed-NCBI	The Cochrane Library	Elsevier	Total
Real-time and Predictive Analytics	real-time analysis OR real-time analytics OR real-time anal* OR predictive analysis OR predictive analytics OR predictive anal*	333835	2403	0	336238
Real-time Analytics and Digital Epidemiology	(real-time analysis OR real-time analytics OR real-time anal* OR predictive analysis OR predictive analytics OR predictive anal*) AND (epidem* OR digital epidem*)	8570	896	0	9466
Maxillary Sinus and Maxillary Teeth	("Molar Teeth" OR "Premolar Teeth" OR "Tooth Extraction" OR "Exodontia") AND ("Maxillary Sinus" OR "Sinus Anatomy" OR "Schneiderian Membrane")	436	5	0	441
Combination of Themes	[(real-time analysis OR real-time analytics OR real-time anal* OR predictive analysis OR predictive analytics OR predictive anal*) AND (epidem* OR digital epidem*)] AND [("Molar Teeth" OR "Premolar Teeth" OR "Tooth Extraction" OR "Exodontia") AND ("Maxillary Sinus" OR "Sinus Anatomy" OR "Schneiderian Membrane") AND ("Sinus Abnormalities" OR "Periapical Abscess" OR "Periodontitis")]	0	1 †	0	1
	Total Number of Hits	342841	3305	0	346146

† Hits were irrelevant to the research questions

1B). Themes included five different topics including "Premolars and Molars", "Maxillary Sinus", "Pathologies", "Surgical Procedures", and "Radiology". We applied different combinations of key words and themes, via the implementation of Boolean Operators (AND, OR, NOT) (16). Bibliographic materials of interest were assessed and appraised for validity and rigorousness via critical appraisal tools (17, 18). Duplicate publications were eliminated, and studies that successfully passed the critical appraisal were deemed as satisfactory reference materials. Those studies were conducted on humans as well as non-human species, and written exclusively in the English language. Priority was given to recently-published literature within the past 5-10 years.

Data were extracted from Google Trends database for the past five years from the 18th of August 2013 to the 18th of August 2018 (19). We used five key words to retrieve raw numerical week-by-week particulars on the temporal trends, geographic mapping, and related queries by web users. Key words included "Schneiderian membrane", "Maxillary Sinus", "Sinus lift",

Table 1B - Investigation of databases of literature: key words *versus* the maxillary sinus.

		Number of Hits			
Theme of key words	Key words	PubMed-NCBI	The Cochrane Library	Elsevier	Total
Premolars and Molars	Molar Teeth	35591	92	23	35706
	Premolar Teeth	14043	40	9	14092
	Tooth Extraction	23824	306	36	24166
	Exodontia	23903	1	9	23913
Maxillary Sinus	Maxillary Sinus	16536	35	52	16623
	Sinus Anatomy	41450	17	185	41652
	Schneiderian Membrane	30189	18	0	30207
Pathologies	Sinus Abnormalities	16032	176	83	16291
	Periapical Abscess	2005	7	7	2019
	Periodontitis	36335	101	269	36705
Surgical Procedures	Candidate Site	9355	247	120	9722
	Endodontics	37412	50	108	37570
	Implant Dentistry	15440	60	101	15601
	Dental Implant	42325	64	230	42619
	Dental Implant Complications	4866	51	35	4952
	Sinus Floor Elevation	832	8	1	841
Radiology	Dental X-Ray	30688	44	43	30775
	OPG	312	3	6	321
	Orthopantomogram	312	14	1	327
Combination of key words within Theme	“Molar Teeth” OR “Premolar Teeth” OR “Tooth Extraction” OR “Exodontia”	24057	74	0	24131
	“Maxillary Sinus” OR “Sinus Anatomy” OR “Schneiderian Membrane”	14878	26	0	14904
	“Sinus Abnormalities” OR “Periapical Abscess” OR “Periodontitis”	32757	102	0	32859
	“Candidate Site” OR “Endodontics” OR “Implant Dentistry” OR “Dental Implant” OR “Dental Implant Complications” OR “Sinus Floor Elevation”	28894	63	0	28957

To be continued →

continued from Table 1B

	"Dental X-Ray" OR "OPG" OR "Orthopantomogram"	6386	3	0	6389
Combination of Themes	**("Molar Teeth" OR "Premolar Teeth" OR "Tooth Extraction" OR "Exodontia") AND ("Maxillary Sinus" OR "Sinus Anatomy" OR "Schneiderian Membrane")**	436	5	0	441
	("Molar Teeth" OR "Premolar Teeth" OR "Tooth Extraction" OR "Exodontia") AND ("Maxillary Sinus" OR "Sinus Anatomy" OR "Schneiderian Membrane") AND ("Sinus Abnormalities" OR "Periapical Abscess" OR "Periodontitis")	26	4	0	30
	("Molar Teeth" OR "Premolar Teeth"OR "Tooth Extraction" OR "Exodontia") AND ("Maxillary Sinus" OR "Sinus Anatomy" OR "Schneiderian Membrane") AND ("Sinus Abnormalities" OR "Periapical Abscess" OR "Periodontitis") AND ("Candidate Site" OR "Endodontics" OR "Implant Dentistry" OR "Dental Implant" OR "Dental Implant Complications" OR "Sinus Floor Elevation") AND ("Dental X-Ray" OR "OPG" OR "Orthopantomogram")	0	0	0	0
	Total Number of Hits	488884	1611	1318	491813

"Endodontics", and "Periodontal disease". Our study is a hybrid of a cross-sectional analysis via an internet snapshot, as well as real-time analytics of the trends. Hence, the level-of-evidence for this study cannot be categorized in correspondence with the Oxford Centre for Evidence-Based Medicine (CEMB) (20). Real-time analysis was attempted via the integration of Python programming language and Microsoft Excel 2016. This concept was never tried as confirmed the complete absence of published literature relevant to the topic of real-time analysis (Table 1B). Statistical analyses and hypotheses testing, descriptive and inferential, were carried out via Microsoft Excel 2016 and the Statistical Package for Social Sciences (SPSS v.24). The implemented statistical tests included the *Analysis of Variance and Covariance* (ANOVA), *Student's t-test*, and *Linear Regression*. An alpha value (α) of 0.05 and a confidence interval of 95% (95% CI) are considered as the cut-off margin for statistical inference. To achieve real-time analytics based on data already available on Google Trends, we wrote a programming script via Python high-level programming language version 3.6.6, 32-bit using Linux Deepin 15.6 (64-bit) and Windows 10 Pro (64-bit) operating systems (21). We applied Thonny version 2.1.21 interpreter, a Python Integrated Development Environment (IDE). The interpreter is a computer program that directly executes the programming script (22, 23). We imported two libraries (modules), Pytrends and OpenPyXl. Those modules are a collection of precompiled routines that a program can use (24, 25).

Results

The systematic inspection of databases of interest of the published literature yielded a total of 491,813 hits distributed as 488884 (PubMed-NCBI), 1611 (the Cochrane Library), and 1318 (Elsevier). The most successful key words to retrieve data addressing the research questions included two combinations of key words seen in bold fonts (Table 1) generating 441 and 30 hits respectively. Exploration of Google Trends database gave data on related queries from users of the surface web. Those queries were not limited to "Maxillary sinus cyst", "Maxillary sinus infection", "Maxillary sinus pain", "Maxillary sinusitis", "Maxillary sinus retention cyst", "Sinus lift surgery", "Sinus graft", "Sinus augmentation", "Dental implants", "Gum disease", "Periodontitis", "Gingivitis", "Gum disease treatment", and "Periodontal treatment". Google Trends also led to accurate data about the geographic mapping (geo-mapping) of the web users queries towards topics of interest in connection with the maxillary sinus, the posterior maxillary teeth, and related oral pathologies. Geo-mapping was limited to forty-seven countries including Japan, Taiwan, Chile, Germany, Ecuador, United Kingdom, Bulgaria, Ireland, Peru, Italy, Spain, Austria, Venezuela, Brazil, Mexico, Colombia, Greece, United States, Australia, Norway, New Zealand, South Korea, Sweden, Switzerland, Portugal, Ukraine, Singapore, Russia, France, Canada, Romania, Belgium, the Netherlands, Philippines, Argentina, South Africa, Egypt, Malaysia, United Arab Emirates, Kingdom of Saudi Arabia, Poland, India, Pakistan, Thailand, Indonesia, Iran, and Turkey. Countries from the Middle East accounted for 10.64% while countries that represented statistical outliers has contributed to 6.38% of the global map. Those outliers were related to the key word "Sinus lift" and included Austria, Romania, and Turkey. Concerning geo-mapping, the "Schneiderian Membrane" generated no hits at all while other key words averaged 2.81 +/- 0.63 (Maxillary sinus), 1.47 +/- 0.39 (Sinus lift), 27.43 +/- 2.76 (Endodontics), and 68.30 +/- 3.14 (Periodontal Disease). Based on Student's t-test statistics, there was a statistically significant difference between all key words with an exception for "Maxillary sinus" *versus* "Sinus lift" (*p-value*=0.091) (Table 2). To be concluded, the surface web users were most interested in periodontal diseases and endodontics.

The temporal trends were variable for the past five years (2013-) (Figure 1), and they averaged 0.02 +/- 0.01 (Schneiderian Membrane), 2.64 +/- 0.04 (Maxillary sinus), 1.27 +/- 0.03 (Sinus lift), 25.59 +/- 0.17 (Endodontics), and 54.38 +/- 0.38 (Periodontal Disease). Statistical outliers co-existed for only two key words, "Endodontics" and "Periodontal disease", during December of each year as well as lately during September and October in 2017. Scattered correlation and regression analysis confirmed a strong positive correlation between the two key words "Endodontics" and "Periodontal disease" (*R score*=0.669, *p-value*<0.001) (Table 3). Besides, other key words also had a significant moderate-to-strong positive linear correlation including "Schneiderian Membrane" and "Sinus Lift" (R=0.166), "Maxillary Sinus" and "Sinus Lift" (0.226), "Maxillary Sinus" and "Endodontics" (0.516), "Maxillary Sinus" and "Periodontal Disease" (0.495), "Sinus Lift" and "Endodontics" (0.330), and "Sinus Lift" and "Periodontal Disease" (0.218). Besides, the Student's t-test calculations confirmed the existence of statistically significant differences (*p-value*<0.001) among all keywords (Table 3). Hence, the summative statistical inference validates that the web users are most interested in endodontics and periodontal diseases.

Python's programming script (Figure 2) enables an automatic retrieval of data from Google Trends based on key words of interest (up to five). The retrieval process is in real-time, and at

Table 2 - Geo-Mapping: paired samples correlation (top) and paired sample student's t-test (bottom).

	Pairs of key words	N	Correlation	Sig.
Pair 1	Schneiderian Membrane & Maxillary Sinus	47	.	.
Pair 2	Schneiderian Membrane & Sinus Lift	47	.	.
Pair 3	Schneiderian Membrane & Endodontics	47	.	.
Pair 4	Schneiderian Membrane & Periodontal Disease	47	.	.
Pair 5	Maxillary Sinus & Sinus Lift	47	-.100	.506
Pair 6	Maxillary Sinus & Endodontics	47	.293	.046
Pair 7	Maxillary Sinus & Periodontal Disease	47	-.445	.002
Pair 8	Sinus Lift & Endodontics	47	.330	.023
Pair 9	Sinus Lift & Periodontal Disease	47	-.398	.006
Pair 10	Endodontics & Periodontal Disease	47	-.979	.000

	Pairs of key words	Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Schneiderian Membrane - Maxillary Sinus	-2.809	4.297	.627	-4.070	-1.547	-4.481	46	.000
Pair 2	Schneiderian Membrane - Sinus Lift	-1.468	2.733	.399	-2.271	-.666	-3.682	46	.001
Pair 3	Schneiderian Membrane - Endodontics	-27.426	18.884	2.754	-32.970	-21.881	-9.957	46	.000
Pair 4	Schneiderian Membrane - Periodontal Disease	-68.298	21.490	3.135	-74.608	-61.988	-21.788	46	.000
Pair 5	Maxillary Sinus - Sinus Lift	1.340	5.317	.776	-.221	2.902	1.728	46	.091
Pair 6	Maxillary Sinus - Endodontics	-24.617	18.098	2.640	-29.931	-19.303	-9.325	46	.000
Pair 7	Maxillary Sinus - Periodontal Disease	-65.489	23.715	3.459	-72.452	-58.526	-18.932	46	.000
Pair 8	Sinus Lift - Endodontics	-25.957	18.165	2.650	-31.291	-20.624	-9.797	46	.000
Pair 9	Sinus Lift - Periodontal Disease	-66.830	22.716	3.313	-73.499	-60.160	-20.169	46	.000
Pair 10	Endodontics - Periodontal Disease	-40.872	40.165	5.859	-52.665	-29.079	-6.976	46	.000

a regular interval (weekly, bi-weekly, monthly, etc.) that can be customized according to the research requirement. The data were self-regulated to be transferred to an Excel spreadsheet template (Microsoft Excel 2016, 64-bits) that had built-in formulae for statistical analysis and multiple hypothesis testing for statistical inference and in real-time. Complimentary statistical analysis was carried out via SPSS. Eventually, we succeeded in generating a real-time stream of inferential analytics.

Discussion

The concept of real-time analysis was never explored before not only within the field of dental

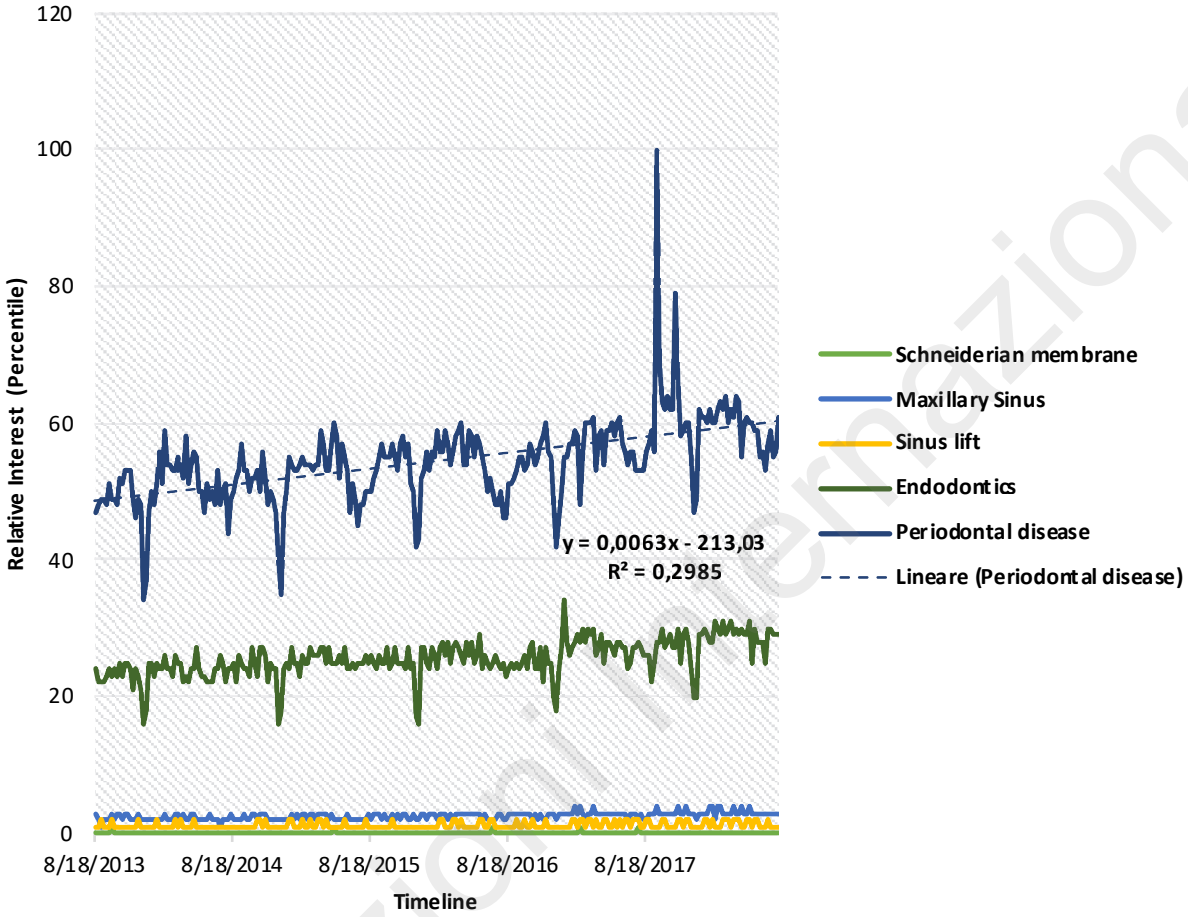

Figure 1
The temporal trends *versus* key words.

anatomy and dental pathology but also in connection with the entire discipline of Dentistry (26). We used key words that are specific to the proposed research questions on the maxillary sinus, maxillary teeth and related oral pathologies (Table 1B). The total number of hits, representing published papers was 346,146, most of which (342,841) were indexed via PubMed-NCBI, and much less (3305) were found on the Cochrane Library, while none existed on Elsevier database. Nevertheless, there was no single study attempting real-time analytics. Hence, there is a full deficit within the existing body of literature about the objectives of this study. Our research is the first of its kind according to which an automated real-time stream of data accompanied by statistical analysis was applicable based on data extrapolated from Google Trends. The digital epidemiological analysis can be applied via online databases of trends. Geographic mapping of the top contributing countries originated mainly from the developed world, as well as few from the Middle East, some Latin countries, and others from Eastern Europe. This study may have some limitations due to the sole reliance on Google Trends as a representative of the databases of trends existing on the surface web. Besides, the retrospective analytic part of the study was specific for a restricted period (2013-2017). Data collected from Google Trends

Table 3 - Temporal trends: paired samples correlation (top) and paired sample student's t-test (bottom).

	Pairs of key words	N	Correlation	Sig.
Pair 1	Schneiderian Membrane & Maxillary Sinus	260	-.010	.871
Pair 2	Schneiderian Membrane & Sinus Lift	260	.166	.007
Pair 3	Schneiderian Membrane & Endodontics	260	.011	.861
Pair 4	Schneiderian Membrane & Periodontal Disease	260	-.055	.377
Pair 5	Maxillary Sinus & Sinus Lift	260	.226	.000
Pair 6	Maxillary Sinus & Endodontics	260	.516	.000
Pair 7	Maxillary Sinus & Periodontal Disease	260	.495	.000
Pair 8	Sinus Lift & Endodontics	260	.330	.000
Pair 9	Sinus Lift & Periodontal Disease	260	.218	.000
Pair 10	Endodontics & Periodontal Disease	260	.669	.000

	Pairs of key words	Paired differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Schneiderian Membrane - Maxillary Sinus	-2.623	.606	.038	-2.697	-2.549	-69.814	259	.000
Pair 2	Schneiderian Membrane - Sinus Lift	-1.254	.445	.028	-1.308	-1.200	-45.452	259	.000
Pair 3	Schneiderian Membrane - Endodontics	-25.569	2.731	.169	-25.903	-25.236	-150.966	259	.000
Pair 4	Schneiderian Membrane - Periodontal Disease	-54.362	6.084	.377	-55.104	-53.619	-144.082	259	.000
Pair 5	Maxillary Sinus - Sinus Lift	1.369	.653	.041	1.289	1.449	33.793	259	.000
Pair 6	Maxillary Sinus - Endodontics	-22.946	2.477	.154	-23.249	-22.644	-149.366	259	.000
Pair 7	Maxillary Sinus - Periodontal Disease	-51.738	5.806	.360	-52.447	-51.029	-143.694	259	.000
Pair 8	Sinus Lift - Endodontics	-24.315	2.616	.162	-24.635	-23.996	-149.889	259	.000
Pair 9	Sinus Lift - Periodontal Disease	-53.108	5.993	.372	-53.840	-52.376	-142.884	259	.000
Pair 10	Endodontics - Periodontal Disease	-28.792	4.707	.292	-29.367	-28.217	-98.629	259	.000

might be occasionally faulty as some web users might be deploying the use of an incognito (hidden) mode of web browsing or dedicated incognito web browsers including Tor Browser, virtual private networks, and internet protocol masking. Subsequent studies should incorporate more than one trends database for cross-validation. Additionally, ventures into the deep web and the darknet should be attempted to recover any relevant data including those on the geographic mapping and temporal trends whenever feasible.

Literature review of relevance to our study

Lozano-Carrascal (2014) confirmed, by means of a cross-sectional analytic study, that CBCT scanning has been shown to be a useful tool for

gtrends.py

```
import pytrends
from pytrends.request import TrendReq
from openpyxl import load_workbook
import time

#Usama_Khalid

def items(wordslist):
    wb = load_workbook('session trends.xlsx')
    ws = wb.active
    mxs=str(1)
    wordslistlen=len(wordslist)
    err=1
    while err==1:
        try:
            ws['A'+mxs] = "Number of day"
            if(wordslistlen>=1):
                ws['B'+mxs] = wordslist[0]
                ws['C'+mxs] =" "
                ws['D'+mxs] =" "
                ws['E'+mxs] =" "
                ws['F'+mxs] =" "
                if(wordslistlen>=2):
                    ws['C'+mxs] = wordslist[1]
                    ws['D'+mxs] =" "
                    ws['E'+mxs] =" "
                    ws['F'+mxs] =" "
                    if(wordslistlen>=3):
                        ws['D'+mxs] = wordslist[2]
                        ws['E'+mxs] =" "
                        ws['F'+mxs] =" "
                        if(wordslistlen>=4):
                            ws['E'+mxs] = wordslist[3]
                            ws['F'+mxs] =" "
                            if(wordslistlen==5):
                                ws['F'+mxs] = wordslist[4]
            wb.save("session trends.xlsx")
            err=0
        except:
            print("Close the file please to add the new data")
            time.sleep(5)
def wrexcel(date,values):
    wb = load_workbook('session trends.xlsx')
    ws = wb.active
    mx=date+1
    mxs=str(mx)
    values_len=len(values)
    err=1
```

Figure 2
The programming script.

evaluating maxillary sinus variations of anatomical parameters including the residual ridge height and width, ridge bone density, maxillary sinus angle, maxillary sinus lateral wall thickness, Schneiderian membrane thickness, maxillary sinus septa, and the posterior superior alveolar artery. CBCT represents the gold standard tool for evaluating the maxillary sinus area (27). Concerning the maxillary septa, Bornstein et al. (2016) studied the analysis of frequency, morphology, and locations of septa using CBCT. Septa are common anatomical structures that often exist in the region of the first or second molar on the floor of the maxillary sinus. Proper pre-operative assessment of the septa, via three-dimensional radiographic examination, is

mandatory to avoid potential complications during sinus floor elevation procedures (28).

In 2015, Bulut et al. studied the relationship between periapical and marginal bone loss and the mucosal thickness of the maxillary sinus in connection with maxillary premolars and molars. Retrospective analysis showed that mucosal thickening (MT) of the maxillary sinus was common among patients with the periodontal bone loss (PBL), and it was significantly associated with apical lesions and PBL (29). Bayrak et al. (2018) conducted another retrospective evaluation and found no statistically significant relationship between nasal septum deviation (NSD) and Schneiderian membrane thickness (SMT). The deviation of the nasal septum existed in 50.6% of patients without gender bias. However, the average SMT was found to be higher in males for all the examined tooth areas (*p-value*≤0.05). The average thickness of the membrane was highest in the first molar region and least in the third molar region (30). Earlier in 2017, Khorramdel et al. published similar data confirming that periapical lesions and periodontal infections in the posterior maxilla were associated with Schneiderian membrane thickening. Besides, there was a significant relationship between the location of the posterior maxillary teeth and the thickness of the Schneiderian membrane (31).

In 2014, a study by Acharya et al. revealed that the incidence of advanced periodontal disease was common among Hong Kong Chinese and Asian Indian subjects who sought tooth replacement. Ethnicity, sex, and sinus membrane thickening affected the available bone height in the region below the maxillary sinus (32). Lu et al. (2012) validated, via CBCT imaging, that the prevalence and the extent of the maxillary sinus mucosal thickening were positively associated with the severity of apical periodontitis. CBCT imaging is invaluable for the assessment of the maxillary sinuses and related teeth primarily molars and premolars. Patients in their seventh decade of life had the highest prevalence of mucosal thickening (33). During the same year, Bornstein et al. explored the characteristics and dimensions of the Schneiderian membrane and apical bone in maxillary molars in patients referred for apical surgery. The thickness of the apical bone and the Schneiderian membrane were generally higher in patients with periapical pathoses (34).

For single-tooth implant replacement in the posterior maxilla, it is often necessary to do an augmentation of the alveolar process to overcome the post-extraction bone resorption. In 2011, Kahnberg presented a technique for a local sinus lift with autogenous bone in a one-stage procedure. The researchers validated that local sinus lift with simultaneous bone augmentation and single-tooth replacement in the posterior maxilla is a predictable method although a certain bone volume reduction around the implant was evident at the 2-year follow-up (35). On the other hand, Taschieri et al. (2014) validated via their experimental trial, that the use of platelet concentrates can be effective in reducing the pain, swelling, and surgery-related side effects (36).

In 2017, Eggmann et al. concluded, based on a systematic review of studies implementing CBCT scans, that periapical lesions in the posterior maxilla are likely to be associated with Schneiderian membrane thickening. On the other hand, the current evidence regarding the relation between periodontal diseases and the appearance of the Schneiderian membrane in CBCT is inconclusive (37). Monje et al. (2016), based on their systematic review and meta-regression analytic of thirty-one studies, reported that the overall mean ± SE of the maxillary Schneiderian membrane thickness (SMT) was 1.17 ± 0.1 mm. The mean SMT for the three-dimensional radiography (3DR) group was 1.33 mm, and 0.48 mm for the histology group. Three-dimensional technologies overestimate the SMT by approximately 2.5 folds in comparison with histologic analysis, yet the difference

between the two measurement methods was not statistically significant. Regression analyses, though statistically insignificant, demonstrated that patient with periodontitis and smoking had thicker SMT. The thicker SMT might be more vulnerable to perforation (*p-value*=0.14). On average, SMT is 1 mm in patients seeking sinus augmentation (38).

Several other pathologies can affect the maxillary sinus and the subjacent alveolar ridge as documented by Evrard, Jham, and Kessler (39-41). Evrard reported a tumor attached to the cemento-enamel junction of an impacted third molar at the region of the maxillary tuberosity. The lesion represented an unusual presentation for an odontogenic myxoma in which an aggressive squamous epithelial component existed, altogether with a mucus-secreting component (39). Jham published a report of a case of an extensive central ossifying fibroma (COF) affecting the maxilla of a 62-year-old patient. The lesion had undefined limits on the right side of the upper alveolar ridge and extending towards the palate. The considerable growth potential of COF manifested in this case by the invasion of the maxillary sinus, nasal cavity and the orbit (40). Kessler reported a case of respiratory epithelial adenomatoid hamartoma of the maxillary sinus. Those hamartomas are rare lesions occurring primarily in the nasal cavity, nasopharynx, and the paranasal sinuses (41).

Availability of data

All data, including the raw data and supplementary materials, are available upon request from the corresponding Author.

Acknowledgements

None.

Conflicts of interest

The Authors have nothing to be declared.

Source of funding

This study is entirely self-funded.

References

1. Mittelstadt B, Benzler J, Engelmann L, Prainsack B, Vayena E. Is there a duty to participate in digital epidemiology?. Life sciences, society and policy. 2018 Dec 1;14(1):9.
2. Adawi M, Bragazzi NL, Watad A, Sharif K, Amital H, Mahroum N. Discrepancies between classic and digital epidemiology in searching for the Mayaro virus: preliminary qualitative and quantitative analysis of Google trends. JMIR public health and surveillance. 2017 Oct;3(4).
3. Al-Imam A. Monitoring and Analysis of Novel Psychoactive Substances in Trends Databases, Surface Web and the Deep Web, with Special Interest and Geo-Mapping of the Middle East. info:eu-repo/semantics/masterThesis [dissertation on the Internet]. United Kingdom: University of Hertfordshire; 2017. Doi: 10.13140/RG.2.2.27636.24961.
4. Al-Imam A. Could Hallucinogens Induce Permanent Pupillary Changes in (Ab) users? A Case Report from New Zealand. Case reports in neurological medicine. 2017;2017.
5. Cervellin G, Comelli I, Lippi G. Is Google Trends a reliable tool for digital epidemiology? Insights from different clinical settings. Journal of epidemiology and global health. 2017 Sep 1;7(3):185-9.
6. Choi H, Varian H. Predicting the present with Google Trends. Economic Record. 2012 Jun 1;88(s1):2-9.
7. Carneiro HA, Mylonakis E. Google trends: a web-based tool for real-time surveillance of disease outbreaks. Clinical infectious diseases. 2009 Nov 15;49(10):1557-64.
8. Nuti SV, Wayda B, Ranasinghe I, Wang S, Dreyer RP, Chen SI, Murugiah K. The use of google trends in health care research: a systematic review. PloS one. 2014 Oct 22;9(10):e109583.
9. Rudmik L, Soler ZM. Medical therapies for adult chronic sinusitis: a systematic review. JAMA. 2015 Sep 1;314(9):926-39.
10. Munhoz L, Júnior RA, Abdala R, Arita ES. Diffusion-

Weighted Magnetic Resonance Imaging of the Paranasal Sinuses: A Systematic Review. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. 2018 Jul 21.
11. Mion M, Zanon A, Marchese-Ragona R. The history of paranasal sinus surgery. Medicina Historica. 2018 Feb 14;1(3):139-46.
12. Chai OH, Song CH. Anatomical Achievement and Thought of Leonardo da Vinci. Korean Journal of Physical Anthropology. 2016 Jun 1;29(2):35-46.
13. Block MS. Sinus augmentation at the time of molar tooth removal: Modification of Jensen technique. Journal of Oral and Maxillofacial Surgery. 2015 Jun 1;73(6):1078-83.
14. Oberli K, Bornstein MM, von Arx T. Periapical surgery and the maxillary sinus: radiographic parameters for clinical outcome. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2007 Jun 1;103(6):848-53.
15. Dagassan-Berndt DC, Zitzmann NU, Lambrecht JT, Weiger R, Walter C. Is the Schneiderian membrane thickness affected by periodontal disease? A cone beam computed tomography-based extended case series. Journal of the International Academy of Periodontology. 2013 Jul;15(3):75-82.
16. Salton G. Developments in automatic text retrieval. Science. 1991 Aug 30;253(5023):974-80.
17. Chan SS. Critical Appraisal of Medical Literature. Hong Kong Journal of Psychiatry. 2001 Dec 1;11 (4):26.
18. Umesh G, Karippacheril JG, Magazine R. Critical appraisal of published literature. Indian journal of anaesthesia. 2016 Sep;60(9):670.
19. Microsoft. Google Trends. https://trends.google.com /trends/explore?date=today%205-y&q=Schneiderian%20membrane,maxillary%20sinus,%2Fm%2F0d0kxy,%2Fm%2F03_mvt,%2Fm%2F0jt43f1 (accessed 8 August 2018).
20. University of Oxford. OCEBM Levels of Evidence. https://www.cebm.net/2016/05/ocebm-levels-of-evidence/ (accessed 8 August 2018).
21. Usama Khalid. Python with Excel. https://www.youtube.com/watch?v=F2KSsalTx1k&feature=youtu.be (accessed 13 July 2018).
22. Scott ML. Programming language pragmatics. Morgan Kaufmann; 2000.
23. Lutz M. Learning Python: Powerful Object-Oriented Programming. " O'Reilly Media, Inc."; 2013 Jun 12.
24. Microsoft. GitHub. https://github.com/GeneralMills/pytrends (accessed 8 August 2016).
25. Gazoni E, Clark C. OpenPyXl. https://openpyxl.readthedocs.io/en/stable/ (accessed 8 August 2016).
26. Ahmed Al-Imam. Real-time Analytics for Big Data: Potentials in Data Science and Medical Research. https://www.researchgate.net/publication/328415500_Real-time_Analytics_for_Big_Data_Potentials_in_Data_Science_and_Medical_Research (accessed 23 October 2018).
27. Lozano-Carrascal N, Salomó-Coll O, Gehrke SA, Calvo-Guirado JL, Hernández-Alfaro F, Gargallo-Albiol J. Radiological evaluation of maxillary sinus anatomy: A cross-sectional study of 300 patients. Annals of Anatomy-Anatomischer Anzeiger. 2017 Nov 1;214:1-8.
28. Bornstein MM, Seiffert C, Maestre-Ferrín L, Fodich I, Jacobs R, Buser D, von Arx T. An analysis of frequency, morphology, and locations of maxillary sinus septa using cone beam computed tomography. Int J Oral Maxillofac Implants. 2016 Mar 1;31(2):280-7.
29. Bulut DG, Sekerci AE, Köse E, Sisman Y. Cone beam computed tomographic analysis of maxillary premolars and molars to detect the relationship between periapical and marginal bone loss and mucosal thickness of maxillary sinus. Medicina oral, patología oral y cirugía bucal. Ed. inglesa. 2015;20(5):10.
30. Bayrak S, Ustaoglu G, Demiralp KÖ, Çakmak ES. Evaluation of the Characteristics and Association Between Schneiderian Membrane Thickness and Nasal Septum Deviation. Journal of Craniofacial Surgery. 2018 May 1;29(3):683-7.
31. Khorramdel A, Shirmohammadi A, Sadighi A, Faramarzi M, Babaloo AR, Shamami MS, Mousavi A, Adhami ZE. Association between demographic and radiographic characteristics of the schneiderian membrane and periapical and periodontal diseases using cone-beam computed tomography scanning: A retrospective study. Journal of dental research, dental clinics, dental prospects. 2017;11(3):170.
32. Acharya A, Hao J, Mattheos N, Chau A, Shirke P, Lang NP. Residual ridge dimensions at edentulous maxillary first molar sites and periodontal bone loss among two ethnic cohorts seeking tooth replacement. Clinical oral implants research. 2014 Dec;25(12):1386-94.
33. Lu Y, Liu Z, Zhang L, Zhou X, Zheng Q, Duan X, Zheng G, Wang H, Huang D. Associations between maxillary sinus mucosal thickening and apical periodontitis using cone-beam computed tomography scanning: a retrospective study. Journal of endodontics. 2012 Aug 1;38(8):1069-74.
34. Bornstein MM, Wasmer J, Sendi P, Janner SF, Buser D, Von Arx T. Characteristics and dimensions of the Schneiderian membrane and apical bone in maxillary molars referred for apical surgery: a comparative radiographic analysis using limited cone beam computed tomography. Journal of endodontics. 2012 Jan 1;38(1): 51-7.
35. Kahnberg KE, Wallström M, Rasmusson L. Local sinus lift for single-tooth implant. I. Clinical and radiographic follow-up. Clinical implant dentistry and related research. 2011 Sep;13(3):231-7.
36. Taschieri S, Corbella S, Tsesis I, Del Fabbro M. Impact of the use of plasma rich in growth factors (PRGF) on the quality of life of patients treated with endodontic

surgery when a perforation of sinus membrane occurred. Oral and maxillofacial surgery. 2014 Mar 1;18(1):43-52.
37. Eggmann F, Connert T, Bühler J, Dagassan-Berndt D, Weiger R, Walter C. Do periapical and periodontal pathologies affect Schneiderian membrane appearance? Systematic review of studies using cone-beam computed tomography. Clinical oral investigations. 2017 Jun 1;21(5):1611-30.
38. Monje A, Diaz KT, Aranda L, Insua A, Garcia-Nogales A, Wang HL. Schneiderian Membrane Thickness and Clinical Implications for Sinus Augmentation: A Systematic Review and Meta-Regression Analyses. Journal of periodontology. 2016 Aug;87(8):888-99.
39. Evrard L, Daelemans P, Glineur R, Vanmuylder N, Louryan S, Dourov N. Myxomatous odontogenic tumor of the maxilla. An unusual case with squamous and mucoproducing epithelial component. Acta stomatologica Belgica. 1997 Jun;94(2):59-62.
40. Jham BC, Duraes GV, Rocha CS. Extensive central ossifying fibroma of the maxilla: a case report with description of an alternative surgical technique. Minerva stomatologica. 2006 Oct;55(10):593-7.
41. Kessler HP, Unterman B. Respiratory epithelial adenomatoid hamartoma of the maxillary sinus presenting as a periapical radiolucency: a case report and review of the literature. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2004 May 1;97(5):607-12.

Correspondence to:
Dr. Ahmed Al-Imam
MBChB (Medicine and Surgery), PG-Cert (Dermoscopy), PG-Dip (Dermatology),
MSc (Dermatology), MSc (Human Anatomy and Physiology), MRes (Neuroscience), Ph.D. (Neuroscience)
- CERVO Brain Research Centre, Faculty of Medicine, University of Laval, Canada
- Department of Anatomy and Cellular Biology, College of Medicine, University of Baghdad
E-mail: tesla1452@gmail.com; ahmed.al-imam.1@ulaval.ca