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OXFORD

# A retrospective study of drugs associated with xerostomia from the Australian Database of Adverse Event Notifications

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## Abstract

**Objectives** Xerostomia is a subjective sensation of dry mouth associated with many medications and increases the risk of tooth decay and other oral complications. The aim of this study was to identify unreported medications associated with dry mouth from the Australian Database of Adverse Event Notifications (ADAEN) from the Therapeutic Goods Administration (TGA) in Australia.

**Methods** This was a descriptive retrospective study. A request was made to the TGA to provide all reports associated with dry mouth. De-identified reports were provided from the commencement of the database in 1971 until June 2020. Drugs were divided into established drugs that are associated with xerostomia in the primary literature and secondary drugs not reported in the primary literature.

**Key findings** There were 1927 individual case reports for dry mouth associated with medications. Of these, there were 1379 reports of established (primary) drugs and 1481 reports of secondary drugs associated with xerostomia. Dry mouth was found to be associated with many medication classes; analgesics, cardiovascular and gastrointestinal drugs had the greatest number of secondary drugs reported.

**Conclusions** A comprehensive list of suspected medications associated with xerostomia has been established. This adds to the growing catalogue of medications associated with dry mouth, where several medications have not previously been identified in the primary literature.

**Keywords:** adverse effect; dental; oral adverse effect; xerostomia.

## Introduction

Xerostomia is a subjective symptom and sensation of oral dryness that may or may not be correlated with reduced salivary flow or production.[1, 2] The antibacterial and antiviral properties in saliva are essential for maintaining oral microbial balance and preventing infections.[3, 4] Other functions of saliva include the lubrication, binding and solubilisation of food.[5] Individuals with dry mouth have an increased risk of dental caries and tooth decay.[1, 6]

Dry mouth can have negative social and emotional impacts on affected individuals, which may reduce their quality of life.[7] Oral health-related quality of life (OHRQoL) considers the impact of oral health on various life dimensions,[8] and xerostomia is negatively associated with OHRQoL as people often experience symptoms such as dryness of mouth, burning sensation in the mouth, difficulties in chewing, swallowing, speaking and wearing of dentures.[7–9] Oral health is responsible for the general state of a person's well-being as it is a vital component of overall health.[10] A systematic review by van de Rijt *et al.*[8] showed individuals who experience problems with chewing have reduced OHRQoL scores due to less food consumption and a more restricted diet.[8]

The prevalence of xerostomia in the Australian population above the age of 15 years is 13.2%.[11] A greater proportion of individuals who experience xerostomia are the elderly and individuals who live in socio-demographically disadvantaged areas.[11] While head and neck radiation therapy and medical conditions are major causes of xerostomia, the most common cause is medication use.[12] Certain medication classes such as anticholinergics, sympathomimetics and antihypertensives elevate the risk of dry mouth as a pharmacodynamic adverse effect.[12] A study also suggested that stimulated whole salivary flow rate is more likely to be affected by factors such as medications when compared with age-related changes.[13]

Different pharmacological mechanisms can cause xerostomia induced by drugs, with the main underlying mechanism being the anticholinergic effects of medications.[14] Anticholinergics, antimuscarinic agents and increased adrenergic activity have an effect on the muscarinic gland receptors, resulting in decreased salivary secretion.[15] However, many drugs are associated with xerostomia with the pharmacological mechanism unknown.[16] The aim of this study is to identify unreported medications associated with dry mouth, from the Australian Database of Adverse Event Notifications (ADAEN).[17]

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## Methods

This study was a retrospective analysis of cases reported to the Australian Database of Adverse Event Notifications, whereby a description between drug exposure and xerostomia was documented. The Therapeutic Goods Administration (TGA) receives reports regarding adverse effects after taking suspected medications, and these publicly available reports are recorded in the ADAEN.[17] The TGA uses the ADAEN to monitor and identify potential medication safety concerns.[17–19] These adverse reaction reports are submitted voluntarily by members of the public, general practitioners or other healthcare professionals and are publicly available. We included all cases recorded in the ADAEN reported to the TGA that had reports associated with xerostomia from the time of voluntary reporting of pharmacovigilance data. The primary outcome was to report the drugs associated with xerostomia as recorded by the TGA. The secondary outcomes were to determine whether these drugs in the ADAEN were already associated with xerostomia as reported in the primary literature, or if there were any new medications associated with xerostomia that had not been previously identified. This was to be able to add to the literature evidence for these new drugs an association with this adverse effect.

The TGA was contacted on 7 September 2020, and a request was made by email for all reports containing the words 'dry mouth', 'dry mucosa', 'tongue dry', 'xerostomia' and 'hyposalivation' from the time voluntary reporting began in 1971. These reports are publicly available through both the TGA website and also on request. The reports were received on 11 September 2020, and the data were provided in an excel spreadsheet of abbreviated, de-identified reports received until 10 June 2020. The first reported case of dry mouth was in 1973.

The de-identified data provided by TGA included a case number individualised for each patient, gender, age, onset date of dry mouth, reported date, if the adverse effect of dry mouth was resolved/ongoing/unknown, a list of suspected medication(s) and concurrent medications.

The TGA allocated drugs that they thought were the cause of dry mouth as 'suspected' drugs and the remaining other medications taken by the patient were listed under 'concomitant' medications. In a comprehensive systematic review, Wolff *et al.*[16] determined a list of medications associated with dry mouth. The authors classified drugs into three categories, namely strong, moderate and weak levels of association with dry mouth, based on the quality of evidence reported in the primary literature.[16] This systematic review[16] was used as a reference in this study to identify drugs from the ADAEN that already have evidence for an association with xerostomia, and drugs reported to be associated with dry mouth with no current evidence from the primary literature. With reference to this systematic review, suspected medications assigned by the TGA which have evidence of causing dry mouth in the Wolff *et al.*[16] review are listed under primary drugs in Table 1. The suspected medications that were not listed in the Wolff *et al.*[16] review are listed in Table 1 as 'secondary' medications. That is, secondary medications were those associated with dry mouth reported in the ADAEN database but were not identified in the systematic review, as these medications have not been associated with dry mouth in the primary literature. Secondary drugs with less than five reported cases are presented in

**Table 1** Reports from the DAEN of implicated drugs in xerostomia (excluding secondary drugs with <5 reports)

| Drug class | Primary drugs[1] | Secondary drugs[2] |
|---|---|---|
| Analgesics | | |
| NSAIDs | | 41 |
| Non-opioid analgesic | | 19 |
| Opioids | 78 | 21 |
| Anti-infectives | | |
| Antibacterials | | |
| Penicillins | | 5 |
| Tetracyclines | | 11 |
| Nitroimidazole | | 11 |
| Other antibacterials | | 20 |
| Anti-fungals | | |
| Other anti-fungals | | 7 |
| Anti-malarial | | |
| Quinolones | 1 | 6 |
| Anti-virals | | |
| Guanine analogues | | 6 |
| Other anti-virals | | 10 |
| Anti-retrovirals | | |
| Nucleoside reverse transcriptase inhibitors (NRTIs) | 3 | |
| Nucleoside analogues | | 6 |
| Cardiovascular drugs | | |
| Anti-arrhythmics | 19 | |
| Antihypertensives | | |
| ACE Inhibitors | 64 | 50 |
| Beta-blockers | 66 | 55 |
| Angiotensin Receptor Blockers | | 33 |
| Other antihypertensives | 69 | 20 |
| Antiplatelets | | 9 |
| Calcium channel blockers | | |
| Dihydropyridine | | 32 |
| Non-dihydropyridine | 35 | |
| Diuretics | | |
| Loop diuretics | 40 | |
| Thiazide diuretics | | 27 |
| Potassium sparing diuretics | 30 | 5 |
| Drugs for dyslipidaemia | | |
| Statins | | 39 |
| Nitrates | | 5 |
| Phosphodiesterase 5 inhibitors | | 8 |
| Endocrine drugs | | |
| Bisphosphonates | 12 | 12 |
| Drugs for osteoporosis | | |
| Other drugs for osteoporosis | | 9 |
| Gastrointestinal drugs | | |
| Anti-diarrhoeals | | |
| Opioid anti-diarrhoeals | | 5 |
| Anti-emetics | | |
| Dopamine antagonists | | 19 |

**Table 1.** Continued

| Drug class | Primary drugs[1] | Secondary drugs[2] |
|---|---|---|
| 5HT3 antagonists | 1 | |
| Other anti-emetics | 26 | 36 |
| Drugs for dyspepsia, reflux and peptic ulcers | | |
| H2 receptor antagonist | | 10 |
| Proton pump inhibitors | | 50 |
| Gastrointestinal lipase inhibitors | 2 | |
| Drugs for inflammatory bowel disease | | |
| TNF-alpha antagonists | | 15 |
| Immunomodulators & antineoplastics | | |
| Platinum compounds | 2 | |
| Drugs for gout | | |
| Xanthine oxidase inhibitors | | 5 |
| Immunosuppressants | | 6 |
| Interferons | | 5 |
| Neurological drugs | | |
| Anti-epileptics | 84 | 19 |
| Anticholinergics | 95 | 29 |
| Drugs for parkinsonism disease | | |
| Dopamine agonist | | 5 |
| Drugs for migraine | | |
| Triptans | | 5 |
| Drugs for other neurological conditions | 8 | |
| Drugs for multiple sclerosis | | 9 |
| Psychotropic drugs | | |
| Anti-anxiety | | |
| Benzodiazepines | 1 | 19 |
| Antidepressants | | |
| Tricyclic antidepressants | 155 | |
| Other antidepressants | 63 | |
| Selective serotonin reuptake inhibitors (SSRIs) | 175 | 7 |
| Serotonin norepinephrine reuptake inhibitors (SNRIs) | 68 | |
| MAO Inhibitors | 6 | |
| MAO type B Inhibitors | 1 | |
| Anti-bipolars | 14 | |
| Antipsychotics | | |
| Phenothiazine antipsychotics | 37 | |
| Other antipsychotics | 65 | |
| Drugs for ADHD | | |
| Psychostimulants | 8 | |
| Non-amphetamine psychostimulants | 2 | |
| Other drugs for Attention Deficit Hyperactivity Disorder | 4 | |
| Drugs for alcohol dependence | 4 | |
| Drugs for nicotine dependence | 70 | 24 |

**Table 1.** Continued

| Drug class | Primary drugs[1] | Secondary drugs[2] |
|---|---|---|
| Hypnotics | 13 | |
| Respiratory drugs | | |
| Anti-asthmatic | | |
| Beta 2 agonist | | 5 |
| Corticosteroids | | 24 |
| Opioid cough suppressants | 3 | 5 |
| Others | | |
| Alpha 2 agonist | 9 | |
| Antihistamines | 14 | 24 |
| Appetite suppressants | 27 | 5 |
| Contraceptives | | 6 |
| Decongestants | 14 | |
| Enzymes | | 7 |
| Plants | | 7 |
| Stimulants | | 26 |
| Supplements/vitamins | | 25 |
| Vaccines | | 55 |
| Vasopressin receptor antagonist | 1 | |

[1]Primary drugs: established drugs association with xerostomia from Wolff *et al.*[16]
[2]Secondary drugs: reported drugs associated with xerostomia from the DAEN reports.

Supplementary Table S2. Drugs that interact with suspected drugs to cause dry mouth were categorised as 'interacting' within the ADAEN and were categorised as primary or secondary drugs accordingly. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist was used to report the study.[20]

As these data were publicly available, ethical approval for this study was not required.

## Results

The ADAEN identified a total of 1927 reported cases of dry mouth associated with medications. The drug classes and corresponding number of case reports are presented in Table 1. The demographic characteristics of reported cases include 1250 females, 616 males and 61 individuals of unspecified gender. The age range included patients under the age of 1 and 97 years. Of the 1927 individuals who experienced dry mouth, there were 1379 reported cases associated with primary drugs, 753 cases classified under high evidence level, 356 cases under moderate evidence level and 270 cases as low evidence. Most primary drugs associated with dry mouth included neurological and psychotropic drugs[16] (Supplementary Table S1). There were 1481 secondary drug classifications, with the results described below, and in Table 1 and Supplementary Tables S1 and S2 (<5 reports). Most patients were taking multiple medications, and dry mouth may have been due to the suspected drugs and reported drug interactions. It is unknown whether drug interactions or disease states led to dry mouth from the data provided.

Analgesics accounted for 7.5% (111/1481) of secondary drugs reported. Non-steroidal anti-inflammatory drugs (NSAIDs) accounted for majority of the reported cases (64

cases), with celecoxib (14 reports) and naproxen (9 reports) reporting the highest number of dry mouth case reports. Opioids were the second most common analgesic class to cause dry mouth (27 reports), with oxycodone contributing to the majority (14 reports) of the cases. Paracetamol accounted for a large majority of cases in non-opioid analgesics (19 reports).

Anti-infectives accounted for 10.3% (152/1481 reports) of secondary drugs reported, with antibacterial agents accounting for most cases (92 reports). However, cardiovascular drugs accounted for 21.1% (313/1481 reports) of secondary drugs reported cases, with antihypertensive medications contributing to more than one-third of the reported cases (162 reports). Angiotensin-converting enzyme inhibitors (ACEIs) attributed to most of the antihypertensive reports (57 reports), with captopril accounting for most cases (38 reports). Angiotensin receptor blocker (ARBs) had the second highest case reports (37 reports) with the majority contributed by irbesartan (14 reports). Calcium channel blockers had the third highest case reports (34 reports). Within cardiovascular drugs, the total number of reported cases involving drugs for dyslipidaemia accounted for 3.6% (53/1481) of the secondary drugs reported cases. Statins accounted for the highest number of cases (46 reports), with most cases related to simvastatin (25 reports).

Endocrine drugs accounted for 4.6% (69/1481) of the secondary drug reported cases. Drugs used to treat osteoporosis were most associated with dry mouth (33 reports). Bisphosphonates accounted for half of the reported cases (17 reports), with zoledronic acid being the main contributor (12 reports). Denosumab also contributed to a relatively high number of case reports (9 reports).

Gastrointestinal drugs accounted for 11.4% (169/1481) of the secondary drug reported cases. Drugs used for dyspepsia, gastric reflux and peptic ulcers contributed the largest proportion of cases (72 reports), with proton pump inhibitors accounting for more than two-thirds of the reported cases (50 reports). Anti-emetics accounted for 61 reported cases with the anticholinergic hyoscine hydrobromide unsurprisingly attributing to more than half of the reported cases (36 reports).

Neurological drugs accounted for 7.8% (116/1481) of the secondary drug reported cases. Anticholinergics had the highest number of reports (36 reports), with benztropine being the main contributor in this drug class (15 reports). Anti-epileptics had the second highest number of reports (25 reports), with carbamazepine (14 reports) attributing to the majority of the cases.

Psychotropic drugs accounted for 4.1% (60/1481) of the secondary drug reported cases. Anti-anxiety drugs had the highest number of cases associated with dry mouth, namely benzodiazepines (31 reports). Diazepam (9 cases), alprazolam (5 reports) and temazepam (5 reports) were the medications commonly reported to induce dry mouth in patients.

Respiratory drugs accounted for 4.9% (72/1481) of the secondary drugs reported cases. Corticosteroids were the most common class of respiratory medications associated with dry mouth (34 reports). Anti-asthmatic medications had the second highest number of reported cases in this category (31 reports), with beta-2 agonist having the highest number of reports (18 reports).

The total number of reported cases involving the use of vaccines, supplements and antihistamines accounted for 22.0% (326/1481) of the secondary drugs. Vaccines were associated with the highest number of reports (75 reports), with most patients experiencing dry mouth with influenza vaccine (30 reports) and hepatitis B vaccine (15 reports).

Given the increasing popularity of complementary medicines in Australia, interestingly supplement use led to a reported 54 cases, with Armaforce supplement associated with the majority of reports (19 reports).

## Discussion

This is the first study to comprehensively present medications recorded from the ADAEN database that have been associated with dry mouth. The analysis shows that dry mouth is associated with many medication classes, reinforcing the fact that xerostomia is commonly associated with medication use and that the pharmacological mechanisms are not all known. Anti-infectives, cardiovascular and gastrointestinal drugs were highly reported secondary drugs, contributing 42.8% of all secondary drugs cases. While most associated medications were consistent with findings from the systematic review, there were many other commonly prescribed medicines from the ADAEN that were found to likely be associated with xerostomia.

## Strengths and Limitations

Patients taking multiple medications in most of these reported cases may result in drug interactions causing dry mouth, and this study does not account for the synergistic or interactive effects of concomitant medications. Secondly, the reported cases do not represent the total number of dry mouth cases after taking these medications as the data are voluntarily submitted. Thirdly, there were several reported cases who fall below the age of 1 year. These cases may have been classified into the incorrect age group given the medications and reactions reported. Furthermore, it is unknown whether confounding factors such as concurrent medical conditions or lifestyle choices (e.g. tobacco smoking) contributed to the dry mouth reports.

Finally, adverse event reporting by health professionals to the TGA is low.[19] Although the majority of prescribing stems from general practice, reports from medical practitioners only made up 4.6% of total reports in the July–December 2019 period.[19] The reason for this decrease is unknown and may be due to a decline in adverse events in the population or changes in reporting behaviours. It is also more likely for healthcare professionals to report severe and life-threatening adverse events as opposed to milder and non-serious adverse effects.[21] With a decline in reporting, there may be more cases of dry mouth associated with these secondary drugs which have not been reported and documented. Nonetheless, in this study, these pharmacovigilance data provide a different source of adverse event reporting to that obtained from pharmaceutical companies during clinical trials. Clinical trials have strict patient inclusion and exclusion criteria, and reports of adverse effects may not be representative of the population.[22] The data from the ADAEN are derived from a broader demographic representation of patients and findings add to identified adverse event profiles obtained from pharmaceutical companies during clinical trials.

The most commonly reported mechanism for dry mouth results from the anticholinergic action of the drugs.[14]

Muscarinic acetylcholine receptors have five different subtypes, and receptors in the periphery mediate cholinergic signals to autonomic organs.[14] In particular, the M3-muscarinic receptors (M3R) mediate parasympathetic cholinergic neurotransmission to the salivary glands.[14] There are various types of other receptors for endogenous substances in the salivary glands, which suggest that salivary glands may contain target systems for many drugs.[14] Alpha 1A, beta 1, M3, histamine 2 and some receptors induce dry mouth by mediating exocytosis through cAMP-protein kinase A pathway.[14] Medications most associated with dry mouth are beta-blockers, tricyclic antidepressants and antipsychotics.[14, 23] Many other drugs have the potential to induce dry mouth; however, the pharmacology and mechanisms associated with dry mouth are either unknown or yet to be fully elucidated.[24]

Many types of antidepressants and antipsychotics reported to the ADAEN were listed as primary drugs. Psychotropic drugs are commonly reported to cause dry mouth, with xerostomia being the most frequently reported oral side effect of most antidepressants.[25] Antidepressants are reported to cause salivary gland hypofunction or may change the threshold for perception of dry mouth.[26] Typical antipsychotics have a strong inhibitory action on dopamine D1 and D2 receptors, and affinity for muscarinic, histamine H1 or alpha A1 receptors, mechanisms commonly associated with xerostomia.[27] Atypical antipsychotics may be less associated with dry mouth due to their selective antagonistic activity against the dopamine D2 receptor.[14, 27] There were four typical antipsychotics reported with dry mouth and among the four medications, trifluoperazine was classified under secondary drugs. More reported cases were associated with atypical antipsychotics. This finding may be possibly due to a larger number of patients being prescribed atypical antipsychotics due to their more favourable side effect profile when compared with typical antipsychotics.

Many patients reported dry mouth with the use of analgesics, in particular opioids and NSAIDs. Dry mouth is a commonly reported side effect seen in patients who take opioids.[16, 28] There were no NSAIDs listed in the review by Wolff *et al*.[16]; however, there were numerous NSAIDs reported in the ADAEN including celecoxib, naproxen, piroxicam and ketoprofen associated with multiple cases. A literature review of randomised controlled studies conducted by Derry *et al*.[29] on the use of oral NSAIDs for cancer pain found that dry mouth and thirst were common adverse events experienced by one in seven participants.[29] However, the underlying mechanism is not known. Many NSAIDs are non-prescription medications that are easily accessible by consumers over the counter. Healthcare professionals should be aware of this possible adverse effect of xerostomia associated with their use when counselling patients.

In this study, association between dry mouth and certain antihypertensive drugs including ACE inhibitors, diuretics and beta-blockers was identified.[30] An estimated 13% of patients taking ACE inhibitors complain of dry mouth.[31] In a prospective observational study by Persson *et al*.,[13] diuretic agents were widely used agents that caused xerostomia.[13] Diuretics and medications used for mental illnesses were comparatively similar in reducing the mean stimulated whole salivary flow rate in a group of elderly subjects.[13] In this study, various diuretics were reported, including hydrochlorothiazide and indapamide.

Numerous H2 receptor antagonist and proton pump inhibitor drugs were associated with dry mouth and were not listed as primary drugs.[16] There are other reports in the literature that identify this association. In a randomised controlled trial performed by Kaviani *et al*.,[32] 41% of recipients who had a H2 receptor antagonist (ranitidine) added to the standard treatment combination of amoxicillin, metronidazole and bismuth derivative experienced dry mouth.[14, 32] Omeprazole was also associated with dry mouth, by reducing salivary flow in some patients on this medication. Ceasing omeprazole was shown to reverse dry mouth effects.[33]

## Future Research

While this study highlights that many medications are associated with xerostomia, it is known that xerostomia is dose-dependent and is associated with an increasing number of medications.[34, 35] Further research can be undertaken to ascertain the effects of polypharmacy and drug combinations so that specific patient groups who will experience xerostomia can be better predicted. While the incidence of polypharmacy is increasing internationally and is associated with negative health outcomes, the effects are confounded by co-morbidities.[36] Thus, understanding which drugs and drug classes are more likely to be associated with this adverse effect is also another area of future research, and this can subsequently influence choices of drugs when deprescribing.[37]

Finally, the case reports do not detail the severity of symptoms experienced by patients. Further research assessing drugs that are more likely to cause severe symptoms and hyposalivation will be useful when reducing doses or choosing to deprescribe unnecessary medications.

## Conclusions

Dry mouth is an adverse effect associated with a wide range of commonly prescribed medicines. Anti-infectives, cardiovascular and gastrointestinal drugs had the most reports, and this study adds to the growing literature regarding the drugs associated with xerostomia. While the pharmacodynamics of dry mouth sequelae is established for some drugs, it is unknown for many others and requires further research. The list of medications identified may be used by clinicians to inform patients of this adverse effect, and the comprehensive table can be used as a reference when developing management plans for patients.

## Supplementary Material

Supplementary data are available at *International Journal of Pharmacy Practice* online.

## Author Contributions

P.J.C. was responsible for the design, analysis and interpretation of the data; drafting of the paper; and giving final approval. M.-W.T. was responsible for the design, analysis and interpretation of the data; drafting the paper; and giving final approval. L.T. was responsible for the conception and design, analysis and interpretation of the data; drafting the paper; and giving final approval. All authors had access to the study data that support this publication.

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## Conflict of Interest

The authors declare that they have no conflicts of interest.

## Data Availability

Data are available on request from the authors.

## References

1. Teoh L, Moses G, McCullough MJ. A review and guide to drug-associated oral adverse effects-dental, salivary and neurosensory reactions. Part 1. *J Oral Pathol Med* 2019; 48: 626–36. https://doi.org/10.1111/jop.12911
2. Oral and Dental Expert Group. *Therapeutic Guidelines: Oral and Dental Version 3*. Melbourne, Australia: Therapeutic Guidelines Ltd, 2019.
3. Marsh PD, Do T, Beighton D et al. Influence of saliva on the oral microbiota. *Periodontol 2000* 2016; 70: 80–92. https://doi.org/10.1111/prd.12098
4. Lynge Pedersen AM, Belstrøm D. The role of natural salivary defences in maintaining a healthy oral microbiota. *J Dent* 2019; 80: S3–S12. https://doi.org/10.1016/j.jdent.2018.08.010
5. Tiwari M. Science behind human saliva. *J Nat Sci Biol Med* 2011; 2: 53–8. https://doi.org/10.4103/0976-9668.82322
6. Alsakran Altamimi M. Update knowledge of dry mouth – a guideline for dentists. *Afr Health Sci* 2014; 14: 736–42. https://doi.org/10.4314/ahs.v14i3.33
7. Villa A, Abati S. Risk factors and symptoms associated with xerostomia: a cross-sectional study. *Aust Dent J* 2011; 56: 290–5. https://doi.org/10.1111/j.1834-7819.2011.01347.x
8. van de Rijt LJM, Stoop CC, Weijenberg RAF et al. The influence of oral health factors on the quality of life in older people: a systematic review. *Gerontologist* 2020; 60: e378–94. https://doi.org/10.1093/geront/gnz105
9. Millsop JW, Wang EA, Fazel N. Etiology, evaluation, and management of xerostomia. *Clin Dermatol* 2017; 35: 468–76. https://doi.org/10.1016/j.clindermatol.2017.06.010
10. Gil-Montoya JA, de Mello AL, Barrios R et al. Oral health in the elderly patient and its impact on general well-being: a nonsystematic review. *Clin Interv Aging* 2015; 10: 461–7. https://doi.org/10.2147/CIA.S54630
11. Jamieson LM, Thomson WM. Xerostomia: its prevalence and associations in the adult Australian population. *Aust Dent J* 2020; 65: S67–70. https://doi.org/10.1111/adj.12767
12. Lysik D, Niemirowicz-Laskowska K, Bucki R et al. Artificial saliva: challenges and future perspectives for the treatment of xerostomia. *Int J Mol Sci* 2019; 20: 3199. https://doi.org/10.3390/ijms20133199.
13. Persson RE, Izutsu KT, Treulove EL et al. Differences in salivary flow rates in elderly subjects using xerostomatic medications. *Oral Surg Oral Med Oral Pathol* 1991; 72: 42–6. https://doi.org/10.1016/0030-4220(91)90187-h
14. Scully C. Drug effects on salivary glands: dry mouth. *Oral Dis* 2003; 9: 165–76. https://doi.org/10.1034/j.1601-0825.2003.03967.x
15. Miranda-Rius J, Brunet-Llobet L, Lahor-Soler E et al. Salivary secretory disorders, inducing drugs, and clinical management. *Int J Med Sci* 2015; 12: 811–24. https://doi.org/10.7150/ijms.12912
16. Wolff A, Joshi RK, Ekstrom J et al. A guide to medications inducing salivary gland dysfunction, xerostomia, and subjective sialorrhea: a systematic review sponsored by the world workshop on oral medicine VI. *Drugs R D* 2017; 17: 1–28. https://doi.org/10.1007/s40268-016-0153-9
17. Australian Government Department of Health TGA. *Database of Adverse Event Notifications (DAEN)*. https://www.tga.gov.au/database-adverse-event-notifications-daen. (3 April 2020, date last accessed).
18. Australian Government Therapeutic Goods Administration. *Reporting Adverse Events*. https://www.tga.gov.au/reporting-adverse-events. Published 2021. (24 February 2022, date last accessed).
19. Martin JH, Lucas C. Reporting adverse drug events to the Therapeutic Goods Administration. *Aust Prescr* 2021; 44: 2–3. https://doi.org/10.18773/austprescr.2020.077
20. Equator Network: Enhancing and Quality and Transparency of Health Research. *The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies*. https://www.equator-network.org/reporting-guidelines/strobe/. Published 2019. (1 October 2020, date last accessed).
21. Matsuda S, Aoki K, Kawamata T et al. Bias in spontaneous reporting of adverse drug reactions in Japan. *PLoS One* 2015; 10: e0126413. https://doi.org/10.1371/journal.pone.0126413
22. Council NHaMR. *Who Can Be Part of a Clinical Trial?* https://www.australianclinicaltrials.gov.au/what-clinical-trial/who-can-be-part-clinical-trial. Published 2015. (24 February 2022, date last accessed).
23. Olver IN. Xerostomia: a common adverse effect of drugs and radiation. *Aust Prescr* 2006; 29: 97108–98. https://doi.org/10.18773/austprescr.2006.063
24. Frydrych AM. Dry mouth: xerostomia and salivary gland hypofunction. *Aust Fam Physician* 2016; 45: 488–92.
25. Cockburn N, Pradhan A, Taing MW et al. Oral health impacts of medications used to treat mental illness. *J Affect Disord* 2017; 223: 184–93. https://doi.org/10.1016/j.jad.2017.07.037
26. Thomson WM. Dry mouth and older people. *Aust Dent J* 2015; 60: 54–63. https://doi.org/10.1111/adj.12284
27. Roganović J. Pharmacodynamic causes of xerostomia in patients on psychotropic drugs. *ACTA Sci Dent Sci* 2018; 2: 102–6.
28. Bruera E, Belzile M, Neumann CM et al. Twice-daily versus once-daily morphine sulphate controlled-release suppositories for the treatment of cancer pain. A randomized controlled trial. *Support Care Cancer* 1999; 7: 280–3. https://doi.org/10.1007/s005200050261
29. Derry S, Wiffen PJ, Moore RA et al. Oral nonsteroidal anti-inflammatory drugs (NSAIDs) for cancer pain in adults. *Cochrane Database Syst Rev* 2017; 7: CD012638.
30. Ramírez Martínez-Acitores L, Hernández Ruiz de Azcárate F, Casañas E et al. Xerostomia and salivary flow in patients taking antihypertensive drugs. *Int J Environ Res Public Health* 2020; 17.
31. Mangrella M, Motola G, Russo F et al. Hospital intensive monitoring of adverse reactions of ACE inhibitors. *Minerva Med* 1998; 89: 91–7.
32 Kaviani MJ, Malekzadeh R, Vahedi H et al. Various durations of a standard regimen (amoxycillin, metronidazole, colloidal bismuth sub-citrate for 2 weeks or with additional ranitidine for 1 or 2 weeks) on eradication of *Helicobacter pylori* in Iranian peptic ulcer patients. A randomized controlled trial. *Eur J Gastroenterol Hepatol* 2001; 13: 915–9. https://doi.org/10.1097/00042737-200108000-00007
33 Teare JP, Spedding C, Whitehead MW et al. Omeprazole and dry mouth. *Scand J Gastroenterol* 1995; 30: 216–8. https://doi.org/10.3109/00365529509093266
34 Storbeck T, Qian F, Marek C et al. Dose-dependent association between xerostomia and number of medications among older adults. *Spec Care Dentist* 2022; 42: 225–31. https://doi.org/10.1111/scd.12662.
35 Viljakainen S, Nykänen I, Ahonen R et al. Xerostomia among older home care clients. *Community Dent Oral Epidemiol* 2016; 44: 232–8. https://doi.org/10.1111/cdoe.12210
36 Wastesson JW, Morin L, Tan ECK et al. An update on the clinical consequences of polypharmacy in older adults: a narrative review. *Expert Opin Drug Saf* 2018; 17: 1185–96. https://doi.org/10.1080/14740338.2018.1546841
37. McQuade BM, Campbell A. Drug prescribing: polypharmacy and deprescribing. *FP Essent* 2021; 508: 33–40.