UNIVERSIDADE FEDERAL DO RIO DE JANEIRO
Centro de Ciências da Saúde
Faculdade de Odontologia
Departamento de Clínica Odontológica

AMANDA VERVLOET DUTRA AGOSTINHO ASSIS

PREVALÊNCIA DE HPV NA CAVIDADE ORAL DE INDIVÍDUOS HIV+ E HIV-. REVISÃO SISTEMÁTICA E METANÁLISE

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Dissertação de Mestrado Profissional apresentada ao Programa de Pós-Graduação em Clínica Odontológica da Faculdade de Odontologia da Universidade Federal do Rio de Janeiro, como parte dos requisitos necessários à obtenção do título de Mestre em Clínica Odontológica.

Orientadoras: Profa. Dra. Gloria Fernanda Barbosa de Araújo Castro

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Dedico este trabalho a **Deus**, o autor da vida!

"Porque dele, e por meio dele, e para Ele são todas as coisas. A Ele, pois, a glória eternamente! Amém."

Romanos 11:36

Aos maiores amores da minha vida:

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pelo amor e irrestrito companheirismo, partilhando momentos de entusiasmo e esmorecimento.

"O amor é paciente, o amor é bondoso. Não inveja, não se vangloria, não se orgulha. Não maltrata, não procura seus interesses, não se ira facilmente, não guarda rancor. O amor não se alegra com a injustiça, mas se alegra com a verdade. Tudo sofre, tudo crê, tudo espera, tudo suporta."

1 Coríntios 13:4-7

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“O coração do homem planeja o seu caminho, mas o Senhor lhe dirige os passos.”

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RESUMO

ASSIS, Amanda Vervloet Dutra Agostinho. Prevalência de HPV na cavidade oral de indivíduos HIV+ e HIV-. Revisão sistemática e metanálise. Rio de Janeiro, 2017. Dissertação (Mestrado Profissional em Clínica Odontológica) – Faculdade de Odontologia, Universidade Federal do Rio de Janeiro, Rio de Janeiro, 2017.

O Papilomavírus Humano (HPV) possui tropismo pelo epitélio cutâneo-mucoso e embora seja mais frequente na região anogenital, também pode ser encontrado na mucosa oral. Em indivíduos portadores de HIV/AIDS, manifestações orais são relatadas como sinal da progressão da infecção e, com o advento da Terapia Antirretroviral Altamente Ativa (HAART), houve uma importante redução em algumas manifestações orais, embora haja aumento em verrugas orais. Dessa forma, o objetivo do presente estudo foi identificar se a prevalência de HPV na cavidade oral é maior em indivíduos infectados pelo HIV (HIV+) do que em não infectados pelo HIV (HIV-), por meio de uma revisão sistemática da literatura e metanálise. Foram incluídos nesta revisão estudos observacionais que realizaram a detecção de HPV, pelo método de PCR, na cavidade oral de indivíduos HIV+ e HIV-, cuja coleta foi realizada por meio de *swab,* escova estéril ou saliva. Uma pesquisa eletrônica abrangente, sem restrições de ano e idioma, foi realizada nas bases de dados: *PubMed*, LILACS, *Scopus, Web of Science, Cochrane Library* e *Open Grey*. Avaliação da qualidade dos artigos incluídos, bem como do risco de viés, foi realizada por meio de qualificador específico para a área médica. Já a metanálise foi realizada por meio do *MedCalc*® - *version 14.8.1*, baseando-se nos efeitos de todos os estudos agrupados (*overall effect*) e no subgrupo relacionado ao tipo de coleta.

Do total de 993 estudos identificados, 13 preencheram os critérios de elegibilidade e foram incluídos na síntese final. Os estudos incluídos foram considerados de “baixo” risco de viés. A metanálise demonstrou que a chance de um indivíduo HIV+ apresentar infecção pelo HPV na cavidade oral foi, aproximadamente, três vezes maior (OR = 2,76; IC 95% = 2,36 - 3,23) do que um indivíduo HIV-, independentemente do método de coleta de amostra biológica ser por meio de *swab*/escova (OR = 3,07; IC 95% = 1,70 - 5,56) ou por saliva (OR = 2,74; IC 95% = 2,33 - 3,22). Diante de tais resultados, conclui-se que há evidência científica que suporte a afirmação de que indivíduos HIV+ apresentam maior prevalência de infecção de HPV na cavidade oral quando comparados a indivíduos HIV-.

Palavras-chave: *Papillomaviridae*, boca, HIV, Revisão Sistemática, Metanálise.

ABSTRACT

ASSIS, Amanda Vervloet Dutra Agostinho. Prevalência de HPV na cavidade oral de indivíduos HIV+ e HIV-. Revisão sistemática e metanálise. Rio de Janeiro, 2017. Dissertação (Mestrado Profissional em Clínica Odontológica) – Faculdade de Odontologia, Universidade Federal do Rio de Janeiro, Rio de Janeiro, 2017.

Human papilomavirus (HPV) exhibts tropism for cutaneous and mucosal epithelium and although it is most common in the anogenital region, it can also be found in the oral mucosa. In HIV/AIDS individuals, oral manifestations has been reported as a sign of disease progression, and since the advent of Highly Active Antiretroviral Therapy (HAART), there was a significant reduction of some oral manifestations while there was an increase in oral warts. Thus, the aim of this study was to identify whether the prevalence of HPV in the oral cavity is higher among HIV-infected (HIV+) individuals than HIV non-infected (HIV-) through a systematic review and meta-analysis. In this review were included observational studies that performed the detection of HPV by the PCR method in the oral cavity of HIV+ and HIV- individuals and the sample collection by swab, sterile brush or saliva. A comprehensive surch, with no year and language restrictions, was performed in PubMed, LILACS, Scopus, Web of Science, Cochrane Library and Open Gray databases. Quality assessment and the risk of bias of the studies included was performed through a specific tool for the medical area. The meta-analysis was performed using MedCalc® version 14.8.1, based on overall effect and on the subgroups analysis according to the type of sample collection. From a total of 993 identified studies, 13 met the eligibility criteria and were included in the final

synthesis. Studies included were considered to be at "low" risk of bias. The meta-analysis showed that the odds of an HIV+ individual presenting HPV infection in the oral cavity was approximately three times higher (OR = 2.76, 95% CI = 2.36-3.23) than an HIV-, independently of the method of biological samples collected with swab/brush (OR = 3.07, 95% CI = 1.70-5.56) or saliva (OR = 2.74, 95% CI = 2, 33 - 3.22). According to these results, it was concluded that there is scientific evidence to support the assertion that HIV+ individuals present a higher prevalence of HPV infection in the oral cavity than HIV- individuals.

Keywords: Papillomaviridae, mouth, HIV, Systematic review, Meta-Analysis.

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LISTA DE ABREVIATURAS E SIGLAS

DNA	*Deoxyribonucleic Acid* - Ácido Desoxirribonucleico
HAART	*Highly Active Antiretroviral Treatment* - Terapia Antirretroviral Altamente Ativa
HIV	*Human Immunodeficiency Virus* - Vírus da Imunodeficiência Humana
HIV-	Soronegativo para o HIV
HIV+	Soropositivo para o HIV
HPV	Papilomavírus Humano
IC	Intervalo de Confiança
LILACS	Literatura Latino-americana e do Caribe em Ciências da Saúde
NA	Não aplicável
OR	Razão de Chances
PCR	*Polymerase Chain Reaction* – Reação em Cadeia Polimerase
PRISMA	*Preferred Reporting Items for Systematic reviews and Meta-Analyses*
SIDA/AIDS	Síndrome da Imunodeficiência Adquirida/ *Acquired Immunodeficiency Syndrome*
UNAIDS	*Joint United Nations Program on HIV/AIDS* - Programa Conjunto das Nações Unidas sobre HIV/AIDS

LISTA DE SÍMBOLOS

<	Menor
I^2	Índice de inconsistência
©	*Copyright*
α	Nível de significância
®	Marca registrada
n	Número
=	Igual
%	Porcentagem

SUMÁRIO

1 INTRODUÇÃO

A Síndrome da Imunodeficiência Adquirida (SIDA/AIDS) e a infecção pelo Vírus da Imunodeficiência Humana (HIV) são problemas de saúde pública mundial. Segundo o Programa Conjunto das Nações Unidas (UNAIDS), no ano de 2015 havia 2,1 milhões de novas infecções pelo HIV em todo o mundo, totalizando 36,7 milhões de pessoas vivendo com HIV, sendo 34,9 milhões de adultos, dos quais 17,8 milhões de mulheres e 1,8 milhão de crianças (< 15 anos) (UNAIDS, 2016). No Brasil, de 1980 a junho de 2016, foram notificados no país 842.710 casos de AIDS; no ano de 2015, foram 32.321. Cerca de 41,1 mil de casos são registrados, anualmente, conforme dados dos últimos cinco anos (BRASIL, 2016).

Com avanços na implementação da Terapia Antirretroviral Altamente Ativa (HAART), que muitas vezes inclui o uso de inibidores de protease, na década de 1990, houve uma melhora na qualidade de vida dos indivíduos com HIV/AIDS e, por conseguinte, diminuição da morbidade e mortalidade, contribuindo com o aumento da sobrevida (LEVI; VITÓRIA, 2002). Porém, mesmo após a introdução da HAART, as manifestações clínicas das infecções nesses pacientes continuam chamando a atenção devido a um amplo espectro de agentes oportunistas que são correlacionados com diversas formas de acometimento na cavidade bucal, incluindo fungos, bactérias e vírus. É válido ressaltar que as manifestações na cavidade bucal são relatadas como os primeiros indicadores da infecção pelo HIV (COOGAN; GREENSPAN; CHALLACOMBE, 2005; HODGSON; GREENSPAN; GREENSPAN, 2006; NAIDOO; CHIKTE, 2004; SANTOS et al., 2001), sendo diretamente relacionadas com o grau de imunossupressão do paciente (CHALLACOMBE et al., 2006; CHIGURUPATI; RAGHAVAN; STUDEN-PAVLOVICH, 1996; COOGAN;

GREENSPAN; CHALLACOMBE, 2005; HODGSON; GREENSPAN; GREENSPAN, 2006; MIZIARA; FILHO; WEBER, 2006), podendo ser caracterizadas como um importante valor diagnóstico da doença (PATTON et al., 1999).

Dentre as lesões bucais associadas à infecção pelo HIV com maior frequência podem ser citadas candidíase bucal, hipertrofia das parótidas, eritema linear gengival, estomatite herpética e úlceras aftosas (CHIGURUPATI; RAGHAVAN; STUDEN-PAVLOVICH, 1996; FREZZINI; LEÃO; PORTER, 2005; LEGOTT, 1992; RAMOS-GOMEZ et al., 1999; SOARES et al., 2004). Outras infecções também podem estar fortemente associadas ao HIV como Sarcoma de Kaposi, Linfoma não-Hodgkin e Leucoplasia Pilosa.

King et al. (2002), relataram um aumento na prevalência de lesões bucais associadas ao Papilomavírus Humano (HPV), como verrugas orais relacionadas possivelmente ao uso de HAART. Segundo os autores, essas lesões podem estar associadas com a redução da carga viral, em resposta aos antirretrovirais após imunossupressão grave, sugerindo uma relação entre verrugas e reconstituição imune.

O HPV trata-se de um vírus de Ácido Desoxirribonucleico (DNA), pertencente à família *Papilomaviridae* (DE VILLIERS et al., 2004) que possui tropismo pelo tecido epitelial e mucoso (LETO et al., 2011). É mais frequente na região anogenital, embora também seja encontrado na mucosa oral. Dentre as manifestações orais associadas ao HPV estão: papiloma, condiloma acuminado, hiperplasia epitelial focal, verruga vulgar, leucoplasia, líquen plano, carcinoma de células escamosas e verrucoso (CHANG et al., 1991). O método empregado para a detecção do HPV como padrão ouro é Reação em Cadeia Polimerase (PCR) (TERAI; TAKAGI, 2001).

Como a infecção pelo HIV tem sido apontada como um fator predisponente para maior incidência de lesões bucais associadas ao HPV (KING et al., 2002), é esperado, portanto, que tais manifestações orais sejam mais frequentes nesses pacientes. No entanto, comprovação científica sobre este fato faz-se necessário, visto que esta pode não ser uma realidade desses pacientes infectados já que o uso da terapia antirretroviral combinada com drogas inibidoras de proteases, utilizada no tratamento da infecção pelo HIV, pode indiretamente influenciar nessa prevalência. Diante do exposto, considerando a importância da infecção pelo HPV em indivíduos infectados pelo HIV, no que diz respeito à progressão e ao prognóstico da doença, o presente estudo propõe estudar, através de uma revisão sistemática, a evidência de uma maior prevalência do HPV na cavidade oral nesses indivíduos.

2 OBJETIVO

Avaliar se a prevalência de Papilomavírus Humano na cavidade oral de indivíduos infectados pelo HIV é maior quando comparada com não infectados por meio de uma revisão sistemática da literatura e metanálise, independentemente do método de coleta biológica por *swab*, escova estéril ou saliva.

3 DESENVOLVIMENTO DA PESQUISA

3.1 Artigo: Prevalência de HPV na cavidade oral de indivíduos HIV+ e HIV-. Revisão sistemática e metanálise

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RESUMO

Com o advento da terapia antirretroviral no tratamento de indivíduos portadores de HIV/AIDS houve importante redução em algumas manifestações orais embora haja aumento em verrugas orais. O objetivo deste estudo foi identificar se a prevalência de HPV na cavidade oral é maior em indivíduos HIV+ quando comparados com HIV-, por meio de revisão sistemática e metanálise. Foram incluídos estudos observacionais que realizaram detecção de HPV na cavidade oral de indivíduos HIV+ e HIV- através de PCR, com amostras coletadas por meio de *swab,* escova estéril ou saliva. As bases de dados: *PubMed*, LILACS, *Scopus, Web of Science, Cochrane Library* e *Open Grey* foram pesquisadas. Para a metanálise utilizou-se o *software MedCalc*® - *version 14.8.1*, baseando-se nos efeitos dos estudos agrupados e no subgrupo relacionado ao tipo de coleta. 993 estudos foram identificados, 13 preencheram os critérios de elegibilidade e foram incluídos na síntese final. A metanálise demonstrou que um indivíduo HIV+ apresenta, aproximadamente, chance três vezes maior de infecção pelo HPV na cavidade oral (OR = 2,76; IC 95% = 2,36 - 3,23) do que um indivíduo HIV-, independentemente da amostra biológica ser por meio de *swab*/escova (OR = 3,07; IC 95% = 1,70 - 5,56) ou saliva (OR = 2,74; IC 95% = 2,33 - 3,22). Conclui-se que há evidência científica que suporte a afirmação de que indivíduos HIV+ apresentam maior prevalência de infecção de HPV na cavidade oral quando comparados a indivíduos HIV-.

Significado clínico: Identificar infecção de HPV na cavidade oral é essencial, principalmente na forma de infecção latente ou subclínica sem manifestação de lesão, a fim de se tomar medidas preventivas para evitar maior comprometimento do sistema imunológico do portador de HIV.

Palavras-chave: *Papillomaviridae*, boca, HIV, Revisão Sistemática, Metanálise.

INTRODUÇÃO

Manifestações bucais têm sido relatadas como sendo os primeiros indicadores da infecção pelo HIV[1-4], estando diretamente relacionadas ao grau de imunossupressão do paciente[1,2,5-7]. No entanto, a implementação da Terapia Antirretroviral Altamente Ativa (HAART), que muitas vezes inclui o uso de inibidores de protease, contribui para uma grande melhora na função imune dos pacientes infectados, diminuindo a mortalidade, a morbidade e a prevalência de infecções oportunistas. Por outro lado, apesar do uso de HAART no tratamento de portadores de HIV reduzir consideravelmente o número das manifestações orais, algumas lesões causadas pelo Papilomavírus Humano (HPV) parecem estar aumentando[8-10].

O HPV está relacionado ao surgimento de vários tipos de lesões, tanto benignas como verruga[11] quanto lesões malignas como carcinoma de células escamosas[12]. Atualmente, mais de 100 tipos de HPV já foram identificados, sendo que 30 tipos estão associados a lesões na cavidade oral[13]. O HPV oral pode-se apresentar na forma de papiloma escamoso, condiloma[14] e hiperplasia oral, e está correlacionado com o surgimento de líquen plano, pênfigo vulgar e carcinoma epidermóide oral. O carcinoma verrucoso, apesar de pouco estudado também é uma forma de apresentação do HPV oral[15,16].

Apesar de já ter sido relatado em alguns estudos a maior prevalência de HPV em pacientes infectados pelo HIV, esta pode não ser uma realidade desses pacientes já que o uso de HAART no tratamento da infecção pelo HIV poderia indiretamente mascarar as manifestações orais de HPV. Portanto, uma comprovação científica sobre este fato faz-se necessário, sendo que a hipótese nula deste estudo é a de que indivíduos infectados pelo HIV (HIV+) não apresentam maior prevalência de HPV na cavidade oral quando comparados aos indivíduos não

infectados pelo HIV (HIV-). Diante do exposto, o objetivo deste estudo foi realizar uma revisão sistemática da literatura e metanálise para determinar a verificação dessa hipótese.

MÉTODOS

Esta revisão sistemática foi registrada na base de dados PROSPERO sob o número CRD 42016049546, seguindo as recomendações do PRISMA (*Preferred Reporting Items for Systematic reviews and Meta-Analyses*)[17] e de Maia e Antonio (2012)[18].

Estratégia de busca na literatura

Foi realizada uma busca sistemática na literatura das seguintes bases de dados eletrônicas: *PubMed, Web of Science, Cochrane Library, Scopus* e LILACS, de acordo com as regras de sintaxe de cada base de dados e utilizando os operadores booleanos “AND” e “OR” para combinações das palavras-chave. As buscas foram realizadas até outubro de 2016 e nenhum filtro foi aplicado nas buscas, não havendo também restrições de idioma e nem de ano. A literatura cinzenta também foi pesquisada. Na Tabela 1 constam as bases de dados eletrônicas pesquisadas e suas respectivas estratégias de busca.

Etapas da seleção da referência

Todas as referências foram importadas para gerenciamento de referência no *software EndNote*© 2014 (Thomson Reuters Inc., Philadelphia, PA, EUA). Primeiramente, dois pesquisadores (AVDA e AM), de forma independente, avaliaram os títulos e resumos dos artigos relacionados pela busca a fim de avaliar os critérios de elegibilidade, excluindo aqueles que não os preenchiam. Posteriormente, realizaram a leitura na íntegra dos artigos potencialmente elegíveis. Se o consenso não fosse atingido, um terceiro avaliador ajudaria neste processo.

Critérios de Elegibilidade

Os critérios de elegibilidade seguiram a estratégia PECO. Foram considerados elegíveis os estudos nos quais foi avaliada a cavidade oral de indivíduos (P) infectados por HIV (E) comparados com indivíduos saudáveis (C) a fim de avaliar o diagnóstico de HPV (O). Dessa forma, para ser incluído, o trabalho deveria: (a) ser um estudo observacional, (b) possuir dados sobre o diagnóstico de HPV oral em indivíduos HIV+ comparados com indivíduos saudáveis, (c) ter feito coleta de material biológico por meio de *swab,* escova estéril ou saliva e (d) ter utilizado a técnica de PCR como método de detecção do HPV. Não houve restrição quanto ao local do recrutamento dos indivíduos (departamentos acadêmicos universitários, hospitais, atenção básica e clínicas particulares).

Ademais, foram excluídos estudos com coletas de material biológico subgengival ou provenientes de lesão associada ao HPV, informações insuficientes, *overllaping* amostral, artigo de revisão, caso clínico, capítulos, editoriais, *guidelines* e artigos cujo desfecho não fosse relacionado à pergunta desta revisão.

Avaliação da qualidade metodológica e de risco de vieses

Estudos que preencheram completamente os critérios de inclusão foram avaliados quanto a sua qualidade metodológica e risco de vieses, seguindo o guia proposto por Fowkes e Fulton (1991)[19] que permite a classificação de estudos de diversos desenhos e natureza. Foram avaliadas questões relacionadas ao desenho do estudo, seleção da amostra e do grupo controle, medida de desfecho e possíveis fatores de confundimento dos resultados. De acordo com a importância da falha ou dos critérios utilizados nos estudos, a avaliação foi realizada da seguinte forma: cada item foi marcado como maior problema (++), menor problema (+) ou ausência de problema (0); para os itens nos quais a questão não era aplicável, "NA" foi registrado. Esse qualificador permite um julgamento sobre a validade interna do estudo, a partir de três perguntas-sumário, que se encontram ao final da Tabela 2, uma vez conhecido se os métodos utilizados foram adequados para gerar informações úteis ou não.

METANÁLISE

Para a realização da metanálise a frequência de infecção por HPV foi comparada em indivíduos HIV+ e HIV-. Estudos que apresentaram risco de viés moderado e baixo foram inseridos na metanálise. Os estudos foram agrupados em sua totalidade a fim de identificar a razão de chances (OR) para a infecção por HPV. Além disso, a análise dos subgrupos foi realizada de acordo com o método de coleta: *swab*/escova ou saliva. Para a análise da heterogeneidade entre os estudos foi empregado o teste *Cohran's Q* e o *I-squared* (I^2). Após ser confirmada a

homogeneidade, utilizou-se o método de *Mantel-Haenszel* (Mantel & Haenszel, 1959)[20] para calcular a razão de chances para a infecção pelo HPV nos subgrupos. O nível de significância adotado foi de 5% (α = 0,05). Os dados foram tabulados e analisados no *MedCalc*® - versão 14.8.1 (*MedCalc Software bvba, Ostend, Belgium*).

RESULTADOS

Foram identificados 993 artigos a partir da pesquisa nos bancos de dados selecionados. Com a remoção de 456 referências duplicadas, permaneceram 537 artigos. Destes, após avaliação por meio de leitura do título e resumo (ou texto completo quando este estava indisponível), foram selecionados 97. Destes, 84 foram excluídos com base nos seguintes critérios: ausência de grupo controle (n = 30); coleta de material biológico não proveniente da cavidade oral, oriundo de lesão ou fluido gengival (n = 11); capítulo/artigo de revisão/relato de caso (n = 15); nota/carta ao editor (n = 4); resumos de artigos publicados (n = 3); mesmo universo amostral (n = 6); informação insuficiente (n = 1); desfecho não relacionado ao tema (n = 14). Sendo assim, 13 artigos foram incluídos nesta revisão. Os resultados das buscas nas bases de dados eletrônicas encontram-se apresentados na Figura 1. A avaliação da qualidade metodológica e de risco de vieses dos estudos incluídos encontra-se na Tabela 2, enquanto seus detalhamentos, no que se refere aos dados extraídos estão apresentados na Tabela 3.

O tamanho da amostra variou de 48 a 52 no caso de crianças e adolescentes e de 33 a 761 entre os adultos, enquanto que a idade compreendida foi de seis a 14 anos para os primeiros, e de 32 a 50 para os últimos. Alguns

estudos foram realizados apenas com mulheres[21-24], outros somente com homens[25-26] e ainda aqueles que avaliaram ambos os sexos entre os adultos[27-31] e entre crianças e adolescentes[32-33].

Em relação à prevalência de HPV na cavidade oral, os resultados mostraram uma maior proporção em portadores de HIV.

Dentre os estudos avaliados, as amostras do material biológico foram coletadas por meio do uso de *swab*[27,32,33], escova[24] ou através da coleta de saliva[21-23,25,26,28-31]. Quanto ao método empregado para a identificação de HPV, foi utilizada a técnica de PCR em todos os estudos.

Quanto ao desenho do estudo, todos os artigos submetidos apresentaram-se adequados para o objetivo do estudo, com exceção de um[30] cujo desenho transversal não permitiu o conhecimento da história de infecção de HPV anterior à infeção por HIV e o desenvolvimento de lesões orais. Dos 13 estudos, apenas quatro eram coorte[21,23,26,28] e nove, avaliações transversais[22,24,25,27,29-33]. No que se refere à representatividade dos estudos, seis informaram que o tamanho da amostra foi baseado em parâmetros de conveniência[21,23,25,28,31,32]. Já em relação ao grupo controle ser aceitável, todos os estudos informaram a fonte da amostra dos pacientes HIV -, sendo que cinco informaram pareamento dos sujeitos de pesquisa por idade[21,27,28,30,33].

Na avaliação da qualidade dentre os aspectos de abrangência, todos os trabalhos encontraram-se como favoráveis. Quanto às influências de distorção, os estudos foram realizados com crianças, adolescentes e adultos de ambos os sexos. As idades variaram de seis a 50 anos, sendo a maioria dos indivíduos HIV- adultos de alto risco, visto que eram oriundos de clínicas de doenças sexualmente transmissíveis.

Após a avaliação, mesmo diante de algumas falhas metodológicas, todos os estudos incluídos nesta revisão puderam ser avaliados positivamente com baixo risco de viés.

Em relação à metanálise, a Figura 2 mostra que um total de 4.582 indivíduos (2.113 HIV- e 2.469 HIV+) foram agrupados na análise geral. Observou-se que a chance de um indivíduo HIV+ apresentar infecção pelo HPV na cavidade oral foi quase três vezes maior (OR = 2,76; IC 95% = 2,36 - 3,23) do que um indivíduo HIV-. O tipo de coleta da amostra biológica não influenciou de forma significativa o resultado da metanálise, visto que a OR para infecção por HPV manteve-se, aproximadamente, três vezes maior para os indivíduos HIV+ *versus* HIV- tanto no subgrupo *swab*/escova (OR = 3,07; IC 95% = 1,70 - 5,56) como no subgrupo saliva (OR = 2,74; IC 95% = 2,33 - 3,22).

DISCUSSÃO

Este é o primeiro trabalho de revisão sistemática e metanálise que avalia a prevalência de HPV na cavidade oral de indivíduos HIV+ quando comparados a indivíduos não infectados. A revisão sistemática é respaldada em avaliações sistemáticas com alta qualidade de estudos metodológicos com o intuito de identificar pesquisas relevantes, publicadas ou não, através de critérios de seleção[18]. Já o estudo de metanálise é capaz de gerar informações baseadas em valores estatísticos mais elevados para qualquer avaliação de interesse.

Nesta revisão, apesar do número considerável de artigos inicialmente encontrados na pesquisa, 13 artigos apresentaram-se elegíveis a fim de avaliar a relação entre infeção de HPV na cavidade oral de indivíduos HIV+ e HIV-. Vale

ressaltar que para ser um artigo elegível tal estudo deveria apresentar um grupo de pacientes HIV+ e outro HIV- e, a partir daí, verificar a presença de HPV na cavidade oral.

Ademais, para artigos diferentes, porém de mesma autoria, apenas permaneceram nesta revisão aqueles cujas amostras eram totalmente independentes, segundo os próprios autores que foram contatados. Adicionalmente, artigos cujas amostras foram oriundas de mesma fonte, de acordo com os próprios autores que foram contatados, embora com desfechos diferentes, foram excluídos desta revisão e elegeu-se aquele com maior universo amostral. Além disso, artigos que tiveram imprecisão na apresentação dos dados com relação à exatidão dos dados referentes à infecção pelo HPV na cavidade oral tiveram que ser excluídos.

Foram incluídos estudos transversais e de coorte, sendo que para os últimos, foram extraídos somente os dados do *baseline*, já que o objetivo do presente trabalho foi investigar a prevalência da infecção de HPV oral em determinado momento e não a sua progressão.

Na descrição dos trabalhos, alguns estudos demonstraram problemas relacionados à inadequação da fonte, tamanho da amostra e amostras pareadas. A dificuldade no recrutamento de pacientes repercute diretamente no pequeno tamanho das amostras, porém o resultado final foi capaz de demonstrar valores confiáveis. Embora o tamanho amostral fosse diminuído, isso não influenciou no resultado desta revisão uma vez que não era objetivo deste estudo verificar associações relacionadas à persistência e a alguns fatores de riscos do HPV, o que não seria possível neste caso. Seis estudos relataram que a amostra dos indivíduos avaliados foi por conveniência[21,23,25,28,31,32] e cinco informaram pareamento/semelhança da amostra por idade[21,27,28,30,33].

Em todos os estudos incluídos, os pacientes infectados pelo HIV deveriam apresentar confirmação da infecção pelo teste *Western Blot*, entretanto em apenas dois trabalhos isso foi realizado[29,33]. Já para o grupo controle, três estudos realizaram o teste *Western Blot* para a confirmação da não infecção pelo HIV[27,29,33]. Um outro estudo utilizou-se de *Dade Behring EnzygnostAntiHIV 1 2 plus Assay (Dade Behring, Marburg, Germany)* e de *Capillus HIV-1/HIV-2 (Trinity Biotech PLC,Wicklow, Ireland)* para confirmação ou não de HIV em ambos os grupos[24].

Quanto à coleta de material para avaliação, a fim de reduzir o potencial de viés e avaliar se a forma de coleta influenciaria na qualidade dos dados, foram realizados dois subgrupos específicos para os diferentes métodos de coleta: *swab*/escova[24,27,32,33] e saliva[21-23,25,26,28-31]. Pode-se notar, por meio da avaliação de metanálise que houve concordância entre os resultados dos artigos encontrados, considerando os diferentes métodos de coleta da amostra biológica. A coleta proveniente de *swab*/escova e saliva não influenciou no resultado, já que a OR para infecção por HPV apresentou-se, aproximadamente, três vezes maior para os indivíduos HIV+ *versus* HIV- tanto no subgrupo *swab*/escova (OR = 3,07; IC 95% = 1,70 - 5,56) como no subgrupo saliva (OR = 2,74; IC 95% = 2,33 - 3,22).

Com relação ao método empregado para a detecção de HPV, todos os estudos avaliaram as amostras pela técnica de PCR, a qual é amplamente utilizada para este fim, sendo considerado padrão ouro devido a sua alta sensibilidade e especificidade[34]. Outros métodos de diagnóstico como microscopia eletrônica, imuno-histoquímica, imunofluorescência e hibridação *in situ* são de baixa e moderada sensibilidade, incluindo o *Southern blot*, *dot blot* e reversa *blot*.

Uma limitação desse estudo pode-se levar em consideração a seleção por apenas estudos que confirmassem o diagnóstico do HPV através da avaliação de

PCR, porém nem todos os centros dispõem de sofisticados métodos de diagnóstico, podendo mascarar de forma a minimizar os resultados encontrados.

Em termos de avaliação da qualidade, com base na ferramenta de colaboração Fowkes e Fulton[19], todos os estudos foram considerados com “baixo” risco de viés desde que se conheceram melhor os requisitos das principais características. A partir dos estudos incluídos na metanálise, todos relataram um desfecho favorável para maior prevalência de HPV na cavidade oral de indivíduos infectados pelo HIV com uma diferença significativa quando comparados ao grupo de soronegativos. Em síntese, os dados agrupados na metanálise baseada nos 13 estudos demonstraram que um indivíduo HIV+ apresenta, aproximadamente, chance três vezes maior de infecção pelo HPV na cavidade oral (OR = 2,76; IC 95% = 2,36 - 3,23) do que um indivíduo HIV-. Como relevância clínica, é importante salientar que a cavidade oral infectada pelo HPV, mesmo na forma de uma infecção latente ou subclínica sem manifestação de lesão, pode atuar como um reservatório para a transmissão do HPV[22,27]. Portanto, é essencial a sua detecção para evitar o comprometimento do sistema imunológico já debilitado do portador de HIV.

CONCLUSÃO

Esta revisão, baseada nas informações científicas disponíveis atualmente, concluiu que indivíduos infectados pelo HIV apresentam maior prevalência de HPV na cavidade oral quando comparados a indivíduos não infectados, independentemente do método de coleta de amostra biológica ser por meio de *swab*, escova estéril ou saliva.

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Tabela 1 - Bases de dados eletrônicas e estratégias de buscas (07/10/2016)

Pubmed

#1 (Acquired Immunodeficiency Syndrome[msh] or Acquired Immunodeficiency Syndrome[tiab] or AIDS[tiab] or HIV Infections[mesh] or HIV Infection*[tiab] or HIV[mesh] or HIV[tiab] or HIV-1[mesh] or HIV-1[tiab] or HIV-2 [mesh] or HIV-2[tiab] or HIV Long-Term Survivors[mesh] or Non Progressor HIV[tiab])	#2 (Mouth [mesh] or mouth [tiab] or Oral Cavit* [tiab] or buccal cavit* [tiab] or Buccal Mucosa[mesh] or Buccal Mucosa[tiab] or Floor of Mouth[tiab] or Mouth mucosa[mesh] or Mouth mucosa[tiab] or Oral Mucosa[tiab] or buccal mucosa[tiab] or oral[tiab])	#3 (Papillomaviridae[mesh] Or Human papillomavirus 6[mesh] or Human papillomavirus 11[mesh] or Human papillomavirus 16 [mesh] or Human papillomavirus 18[mesh] or Human papillomavirus 31[mesh] OR HPV[TIAB] or Papilloma[mesh] or Papilloma*[tiab] or Papilloma, Choroid Plexus[mesh] or Papilloma, Inverted[mesh])

#1 AND #2 AND #3

Scopus and Web of Science

#1 (“Acquired Immunodeficiency Syndrome” OR “AIDS” OR “HIV Infection” OR “HIV infections” OR HIV OR “HIV-1” OR “HIV-2” OR “HIV Long-Term Survivors OR Non Progressor HIV”)	#2 (mouth OR “oral Cavit” OR “oral cavity” OR “buccal cavit” OR “buccal cavity” OR “Buccal Mucosa” OR “Floor of Mouth” OR “Mouth mucosa” OR “oral Mucosa” OR “buccal mucosa” OR “oral”)	#3 (Papillomaviridae OR “Human papillomavirus 6” OR “Human papillomavirus 11” OR “Human papillomavirus 16” OR “Human papillomavirus 18” OR “Human papillomavirus 31” OR HPV OR Papilloma OR Papilloma OR Papillomas OR “Papilloma, Choroid Plexus” OR “Papilloma, Inverted”)

#1 AND #2 AND #3

Tabela 1 - Bases de dados eletrônicas e estratégias de buscas (07/10/2016)

Lilacs/BBO

#1 (tw:((tw:(MH:“Acquired Immunodeficiency Syndrome”)) OR (tw:(MH:HIV Infections)) OR (tw:(MH:HIV Long-Term Survivors)) OR (tw:(MH:HIV-1)) OR (tw:(MH:HIV-2)) OR (tw:(Acquired Immunodeficiency Syndrome)) OR (tw:(Síndrome de Inmunodeficiencia Adquirida)) OR (tw:(AIDS)) OR (tw:(HIV Infection$)) OR (tw:(Infecciones por VIH)) OR (tw:(Infecções por HIV)) OR (tw:(HIV)) OR (tw:(VIH)) OR (tw:(HIV-1)) OR (tw:(VIH-1)) OR (tw:(HIV-2)) OR (tw:(VIH-2))))

#2 MH:Mouth OR MH:”Buccal Mucosa” OR MH:Mouth mucosa OR mouth OR boca OR Oral Cavit$ OR cavidade oral OR buccal cavit$ OR cavidade bucal OR Buccal Mucosa OR mucosa buccal OR Floor of Mouth OR Soalho Bucal OR Suelo de la Boca OR Mouth mucosa OR Oral Mucosa OR buccal mucosa OR oral

#3 (MH:Papillomaviridae OR MH:”Human papillomavirus 6” OR MH:”Human papillomavirus 11” OR MH:“Human papillomavirus 16” OR MH:“Human papillomavirus 18” OR MH:“Human papillomavirus 31” OR MH:Papilloma OR MH:“Papilloma, Choroid Plexus” OR MH:“Papilloma, Inverted” OR HPV OR Papilloma$ OR Papiloma)

#1 AND #2 AND #3

Cochrane

#1 MeSH descriptor: [Acquired Immunodeficiency Syndrome] explode all trees
#2 "Acquired Immunodeficiency Syndrome" or "AIDS"
#3 #1 or #2
#4 MeSH descriptor: [HIV Infections] explode all trees
#5 "HIV Infection" or "HIV infections"
#6 #4 or #5
#7 MeSH descriptor: [HIV] explode all trees
#8 HIV
#9 #7 or #8
#10 MeSH descriptor: [HIV-1] explode all trees
#11 "HIV-1"
#26 #24 or #25
#27 #20 or #23 or #26
#28 MeSH descriptor: [Papillomaviridae] explode all trees
#29 "HPV"
#30 #28 or #29
#31 MeSH descriptor: [Human papillomavirus 6] explode all trees
#32 MeSH descriptor: [Human papillomavirus 11] explode all trees
#33 MeSH descriptor: [Human papillomavirus 16] explode all trees
#34 MeSH descriptor: [Human papillomavirus 18] explode all trees
#35 MeSH descriptor: [Human papillomavirus 31] explode all trees
#36 MeSH descriptor: [Papilloma] explode all trees
#37 "Papilloma*"

Tabela 1 - Bases de dados eletrônicas e estratégias de buscas (07/10/2016)

#12 #10 or #11
#13 MeSH descriptor: [HIV-2] explode all trees
#14 "HIV-2"
#15 #13 or #14
#16 MeSH descriptor: [HIV Long-Term Survivors] explode all trees
#17 #3 or #6 or #9 or #12 or #15 or #16
#18 MeSH descriptor: [Mouth] explode all trees
#19 "mouth" or "Oral Cavit" or "oral cavits" or "buccal cavit" or "buccal cavits"
#20 #18 or #19
#21 MeSH descriptor: [Mouth Mucosa] explode all trees
#22 "Buccal Mucosa" or "Floor Mouth"
#23 #21 or #22
#24 MeSH descriptor: [Mouth Mucosa] explode all trees
#25 "Mouth mucosa" or "Oral Mucosa" or "buccal mucosa" or oral
#38 #36 or #37
#39 MeSH descriptor: [Papilloma, Choroid Plexus] explode all trees
#40 MeSH descriptor: [Papilloma, Inverted] explode all trees
#41 #30 or #31 or #32 or #33 or #34 or #35 or #38 or #39 or #40
#42 #17 and #27 and #41

Sigle

#1 (“Acquired Immunodeficiency Syndrome” OR “AIDS” OR “HIV Infection” OR “HIV infections” OR HIV OR “HIV-1” OR “HIV-2” OR “HIV Long-Term Survivors OR Non Progressor HIV”)

#2 (mouth OR “oral Cavit” OR “oral cavity” OR “buccal cavit” OR “buccal cavity” OR “Buccal Mucosa” OR “Floor of Mouth” OR “Mouth mucosa” OR “oral Mucosa” OR “buccal mucosa” OR “oral”)

(Papillomaviridae OR ”Human papillomavirus 6” OR ”Human papillomavirus 11” OR:“Human papillomavirus 16” OR “Human papillomavirus 18” OR “Human papillomavirus 31” OR Papilloma OR “Papilloma, Choroid Plexus” OR “Papilloma, Inverted” OR HPV OR Papilloma OR Papillomas)

#1 AND #2 AND #3

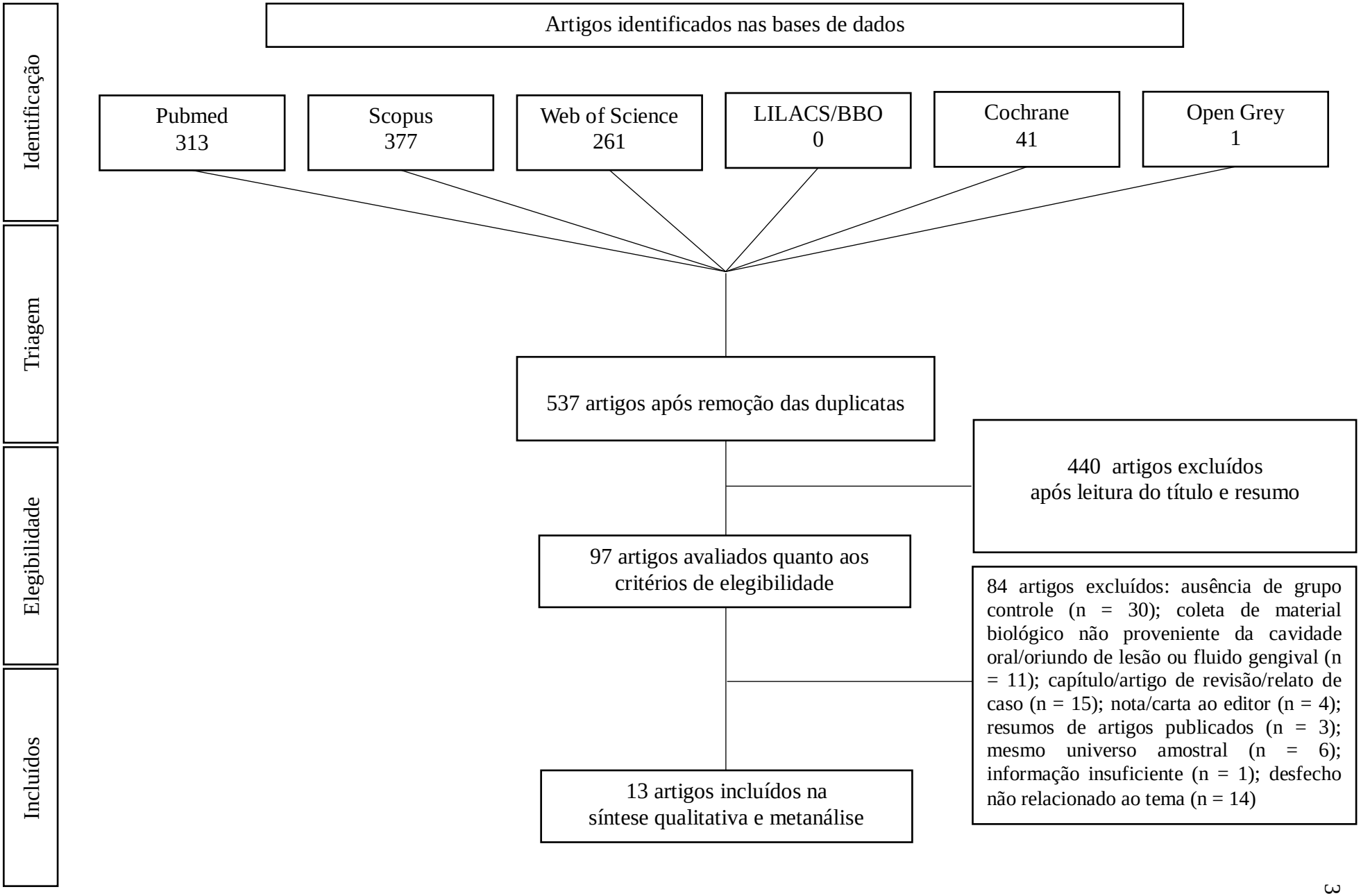

Figura 1 - Diagrama de fluxo do estudo

Tabela 2 - Avaliação da qualidade metodológica e de risco de viés dos 13 estudos, de acordo com as orientações descritas por Fowkes e Fulton[19]

Orientações	*Checklist*		BEACHLER, D. C. et al. 2015	COLON-LOPEZ, V. et al. 2014	COUTLEE, F. et al. 1997	D'SOUZA, G. et al. 2007	FAKHRY, C. et al. 2005	FAKHRY, C. et al. 2006	KREIMER, A. R. et al. 2004	MARAIS, D. J. et al. 2008
O desenho do estudo é adequado ao seu objetivo?	Objetivo	Desenho comum								
	Prevalência	Transversal	-	0	0	-	-	0	0	0
	Prognóstico	Coorte	-	-	-	-	-	-	-	-
	Tratamento	Ensaio controlado	-	-	-	-	-	-	-	-
	Causa	Coorte, caso-controle, transversal	0	-	-	0	0	-	-	-
A amostra do estudo é representativa?	Fonte da amostra		+	+	+	0	0	0	+	0
	Método de amostragem		+	+	0	+	0	+	0	0
	Tamanho da amostra		0	+	0	+	0	0	0	+
	Critérios de inclusão/exclusão		0	0	0	0	0	0	0	0
	Não respondentes		0	0	0	0	0	0	0	0
O grupo controle é aceitável?	Definição de controles		+	+	0	+	+	0	0	0
	Fonte dos controles		0	0	0	0	0	0	0	0
	Correspondência/randomização		0	+	0	0	0	+	+	+
	Características comparáveis		0	0	0	0	0	0	0	0
Qualidade das medidas e dos desfechos?	Validade		0	0	0	0	0	0	0	0
	Reprodutibilidade		0	0	0	0	0	0	0	0
	Cegamento		NA	NA	NA	NA	NA	NA	NA	NA
	Controle de Qualidade		0	0	0	0	0	0	0	0
Integralidade?	Conformidade		0	0	0	0	0	0	0	0
	Perdas		NA	NA	NA	NA	NA	NA	NA	NA
	Mortes		NA	NA	NA	NA	NA	NA	NA	NA
	Dados perdidos		0	0	0	0	0	0	0	0
Influências de distorção?	Outros tratamentos		0	0	0	0	0	0	0	0
	Contaminação		NA	NA	NA	NA	NA	NA	NA	NA
	Mudanças ao longo do tempo		NA	NA	NA	NA	NA	NA	NA	NA
	Fatores de confundimento		+	+	+	+	+	+	+	+
	Distorção reduzida por análise		0	0	0	0	0	0	0	0
Questões-sumário	Viés - Os resultados são erroneamente induzidos em uma determinada direção?		No	No	No	No	No	No	No	No
	Confundimento - Há algum fator de confundimento grave ou influências de distorção?		No	No	No	No	No	No	No	No
	Acaso - É provável que os resultados tenham ocorrido por acaso?		No	No	No	No	No	No	No	No

++, Maior problema; +, menor problema; 0, sem problema; NA, não aplicável; No, não

Tabela 2 (continuação)

Orientações	*Checklist*		MOOIJ, S. H. et al. 2013	MOSCICKI, A. B. et al. 2014	MULLER, K. et al. 2015	PINHEIRO, R. S. et al.2011	VACHAROTAYANGUL, P. et al. 2015
O desenho do estudo é adequado ao seu objetivo?	Objetivo	Desenho comum					
	Prevalência	Transversal	-	0	-	0	0
	Prognóstico	Coorte	-	-	-	-	-
	Tratamento	Ensaio controlado	-	-	-	-	-
	Causa	Coorte, caso-controle, transversal	0	-	+	-	-
A amostra do estudo é representativa?	Fonte da amostra		0	0	+	+	0
	Método de amostragem		0	+	0	+	+
	Tamanho da amostra		0	+	+	+	0
	Critérios de inclusão/exclusão		0	0	0	0	0
	Não respondentes		0	0	0	0	0
O grupo controle é aceitável?	Definição dos controles		+	+	+	0	+
	Fonte dos controles		0	0	0	0	0
	Correspondência/randomização		+	+	0	0	+
	Características comparáveis		0	0	0	0	0
Qualidade das medidas e dos desfechos?	Validade		0	0	0	0	0
	Reprodutibilidade		0	0	0	0	0
	Cegamento		NA	NA	NA	NA	NA
	Controle de qualidade		0	0	0	0	0
Integralidade?	Conformidade		0	0	0	0	0
	Perdas		NA	NA	NA	NA	NA
	Mortes		NA	NA	NA	NA	NA
	Dados perdidos		0	0	0	0	0
Influências de distorção?	Outros tratamentos		0	0	0	0	0
	Contaminação		NA	NA	NA	NA	NA
	Mudanças ao longo do tempo		NA	NA	NA	NA	NA
	Fatores de confundimento		+	+	+	+	+
	Distorção reduzida por análise		0	0	0	0	0
Questões-sumário	Viés - Os resultados são erroneamente induzidos em uma determinada direção?		No	No	No	No	No
	Confundimento - Há algum fator de confundimento grave ou influências de distorção?		No	No	No	No	No
	Acaso - É provável que os resultados tenham ocorrido por acaso?		No	No	No	No	No

++, Maior problema; +, menor problema; 0, sem problema; NA, não aplicável; No, não

Tabela 3 - Resumo dos 13 estudos desta revisão sistemática

Autor, ano	Participantes				Média de idade dos participantes (anos)		Amostra de material biológico	Tipo de identificação	Identificação do HPV			
	HIV+		HIV-									
	Fonte da amostra	Tamanho da amostra	Fonte da amostra	Tamanho da amostra	HIV+	HIV-			HIV+	HIV-	p-valor	Análise estatística
BEACHLER, D. C. et al. 2015	Coorte de estudo Multicêntrico da AIDS (MACS): Chicago, Illinois;Washington, DC/Baltimore, Maryland; Pittsburgh, Pennsylvania e participantes de estudo de Interagência de mulheres com HIV (WIHS): Chicago, Bronx (Nova York) e Brooklyn (Nova York)	761	Coorte de estudo Multicêntrico da AIDS (MACS): Chicago, Illinois;Washington, DC/Baltimore, Maryland; Pittsburgh, Pennsylvania e participantes de estudo de Interagência de mulheres com HIV (WIHS): Chicago, Bronx (Nova York) e Brooklyn (Nova York)	469	47	49	Saliva	PCR	266 (35%)	94 (20%)	-	Teste Qui-quadrado
COLON-LOPEZ, V. et al. 2014	Clínica de doenças sexualmente transmissíveis (DST) em San Juan, Porto Rico	103	Clínica de doenças sexualmente transmissíveis (DST) em San Juan, Porto Rico	101	38.5 (±14.2)	38.5 (±14.2)	Saliva	PCR	23 (22.3%)	18 (17.8%)	p = 0.422	Testes Qui-quadrado e Fisher
COUTLEE, F. et al. 1997	Quatro clínicas de doenças sexualmente transmissíveis e uma clínica de endoscopia gastrointestinal	201	Quatro clínicas de doenças sexualmente transmissíveis e uma clínica de endoscopia gastrointestinal	114	36.7 (±9.3)	36.7 (±9.3)	*Swab*	PCR	29 (14.4%)	3 (2.6%)	p = 0.001	Teste Qui-quadrado
D'SOUZA, G. et al. 2007	Coorte de WIHS	123	Coorte de WIHS	59	-	-	Saliva	PCR	30 (24%)	5 (8.5%)	p = 0.016	Teste Qui-quadrado
FAKHRY, C. et al. 2005	Subgrupo de uma coorte de WIHS	173	Subgrupo de uma coorte de WIHS	87	-	-	Saliva	PCR	40 (23.3%)	7 (8.3%)	p = 0,004	-
FAKHRY, C. et al. 2006	Participantes de cinco lugares de WIHS: Chicago, Ill.; São Francisco, Calif.; Brooklyn, N.Y.; Bronx, N.Y.; Columbia	143	Participantes de cinco lugares de WIHS: Chicago, Ill.; São Francisco, Calif.; Brooklyn, N.Y.; Bronx, N.Y.; Columbia	78	41	40	Saliva	PCR	36 (25.2%)	7 (9.0%)	p < 0.001	Teste Qui-quadrado

Tabela 3 - Resumo dos 13 estudos desta revisão sistemática

Autor, ano	Participantes				Média de idade dos participantes (anos)		Amostra de material biológico	Tipo de identificação	Identificação do HPV			
	HIV+		HIV-									
	Fonte da amostra	Tamanho da amostra	Fonte da amostra	Tamanho da amostra	HIV+	HIV-			HIV+	HIV-	p-valor	Análise estatística
KREIMER, A. R. et al. 2004	Um centro de comunidade hispânica, um programa de reabilitação de drogas, uma clínica médica para indivíduos infectados pelo HIV e um centro de saúde da comunidade em Baltimore	190	Um centro de comunidade hispânica, um programa de reabilitação de drogas, uma clínica médica para indivíduos infectados pelo HIV e um centro de saúde da comunidade em Baltimore	396	43.5	38.4	Saliva	PCR	48 (25.3%)	30 (7.6%)	p < 0.001	Testes Qui-quadrado e Fisher
MARAIS, D. J. et al. 2008	Clínica de colposcopia no Hospital Groote Schuur, Cape Town, África do Sul	33	Clínica de colposcopia no Hospital Groote Schuur, Cape Town, África do Sul	72	32.8	36.7	Escova	PCR	11 (33%)	17 (23.6%)	p = 0.3	Teste Qui-quadrado e de Student
MOOIJ, S. H. et al. 2013	Estudo de coorte em Amsterdam (ACS) entre homens que fazem sexo com homens (serviço de saúde pública de Amsterdam), uma clínica de DST (serviço de saúde pública de Amsterdam), uma clínica de doenças infecciosas (Centro Médico de Jan van Goyen), Amsterdam, Holanda	314	Estudo de coorte em Amsterdam (ACS) entre homens que fazem sexo com homens (serviço de saúde pública de Amsterdam), uma clínica de DST (serviço de saúde pública de Amsterdam), uma clínica de doenças infecciosas (Centro Médico de Jan van Goyen), Amsterdam, Holanda	453	45.6	37.6	Saliva	PCR	178 (56.7%)	125 (27.6%)	p < 0.001	Teste Qui-quadrado
MOSCICKI, A. B. et al. 2014	Centro de Tratamento e Diagnóstico Infantil em Ft. Lauderdale	48	Centro de Tratamento e Diagnóstico Infantil em Ft. Lauderdale	52	14.3 (±3.9)	6.2 (±4.8)	*Swab*	PCR	5 (10%)	1 (2%)	-	Testes Qui-quadrado e Fisher
MULLER, K. et al. 2015	Clínicas de Odontologia, Otorrinolaringologia, Medicina Oral e Cirurgia Oral no Centro Médico	161	Clínicas de Odontologia, Otorrinolaringologia, Medicina Oral e Cirurgia Oral no Centro Médico	128	50.8	50.8	Saliva	PCR	52 (32%)	20 (16%)	p = 0.002	Teste Qui-quadrado

Tabela 3 - Resumo dos 13 estudos desta revisão sistemática

Autor, ano	Participantes				Média de idade dos participantes (anos)		Amostra de material biológico	Tipo de identificação	Identificação do HPV			
	HIV+		HIV-									
	Fonte da amostra	Tamanho da amostra	Fonte da amostra	Tamanho da amostra	HIV+	HIV-			HIV+	HIV-	p-valor	Análise estatística
PINHEIRO, R. S. et al.2011	Montefiore (Bronx, Nova Iorque) e Faculdade de Medicina Dental de Rutgers (Newark, Nova Jersey) Clínica de Pediatria/Imunologia da Universidade Federal do Rio de Janeiro (UFRJ) e Projeto SIDA/AIDS da Faculdade de Odontologia da UFRJ, Brasil	50	Montefiore (Bronx, Nova Iorque) e Faculdade de Medicina Dental de Rutgers (Newark, Nova Jersey) Clínica de Odontopediatria da UFRJ, Brasil	50	9.1 (±2.86)	7.6 (±2.94)	*Swab*	PCR	6 (12%)	3 (6%)	p = 0.24	Teste exato de Fisher
VACHAROTA YANGUL, P. et al. 2015	Clínica anônima da Cruz Vermelha em Bangkok, Tailândia	169	Clínica anônima da Cruz Vermelha em Bangkok, Tailândia	54	36.25 (±7.38)	32.83 (±8.61)	Saliva	PCR	29 (17.16%)	3 (5.56%)	p =0.0346	-

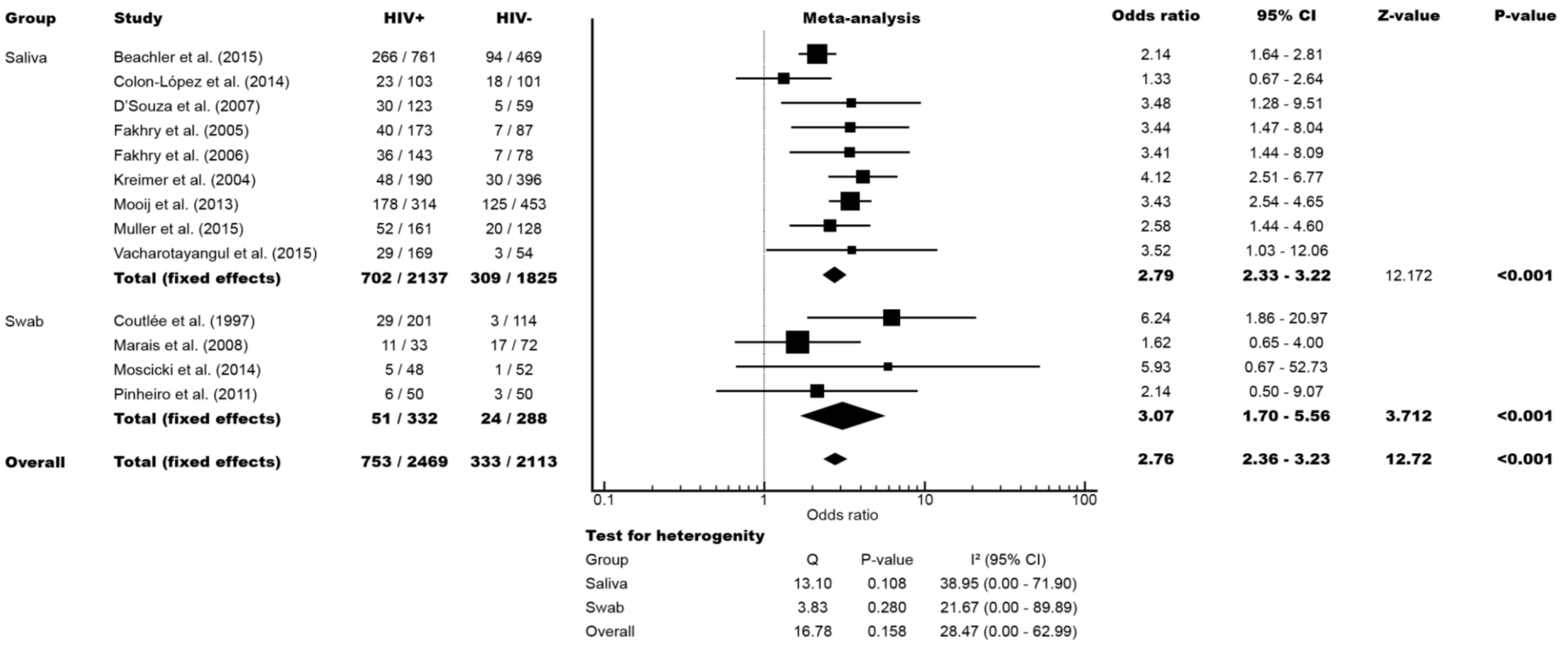

Figura 2 - Forest plot da detecção de HPV oral em indivíduos HIV+ e HIV- dos 13 estudos

4 CONCLUSÃO

De acordo com os dados disponíveis, concluiu-se que indivíduos infectados pelo HIV apresentam maior prevalência de HPV na cavidade oral quando comparados a indivíduos não infectados, independentemente de o método de coleta de amostra biológica ser por meio de *swab*, escova estéril ou saliva.

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6 ANEXO

ANEXO A – Instruções aos Autores do Periódico

ORAL SURGERY, ORAL MEDICINE, ORAL PATHOLOGY AND ORAL RADIOLOGY

The Official Publication for the American College of Oral and Maxillofacial Surgery, American Academy of Oral and Maxillofacial Radiology, American Academy of Oral Medicine, and the American Academy of Oral and Maxillofacial Pathology

GUIDE FOR AUTHORS

Section Scope Statements

The *Oral and Maxillofacial Surgery Section* aims to publish an extensive range of original articles that advances patient care through enhanced understanding of diagnosis, surgical and adjunctive treatment of diseases, and injuries and defects involving both the functional and esthetic aspects of the hard and soft tissues of the oral and maxillofacial regions. The section also seeks research regarding both the basic science of and management of persons with oral and maxillofacial conditions. Articles presenting ethical, original, well-documented, and reproducible research are given preference.

The *Oral Medicine Section* aims to publish a broad range of original articles that help clinicians understand more thoroughly the pathobiology, etiology, diagnosis, prevention, and management of oral conditions related to underlying medical conditions, including diseases of the head, neck, and oral mucosal structures, orofacial pain conditions, salivary gland disorders, and taste disorders. The section also seeks research regarding the dental management of persons with medical problems and/or complicated medical conditions. The published findings must contribute substantively to the body of oral medicine literature and should lead to improved clinical decision-making and enhanced care of medically-related disorders or conditions affecting the oral and maxillofacial region. Articles presenting original, well-documented, and reproducible research are preferred.

The *Oral and Maxillofacial Pathology Section* encourages the submission of original articles of high scientific quality that investigate the pathogenesis, diagnosis, and management of diseases affecting the oral and maxillofacial region. Submitted manuscripts may summarize findings from clinical, translational, or basic research in the broad field of oral and maxillofacial pathology but must contribute substantively to the body of knowledge in this field and should be of obvious clinical and/or diagnostic significance to the practicing oral and maxillofacial pathologist. Areas of focus may include the investigation of disease pathogenesis, the diagnosis of disease using microscopic, clinical, radiographic, biochemical, molecular, or other methods as well as the natural history and management of patients with various conditions of the head, neck, and oral mucosal structures. Diagnostic accuracy studies should conform to the principles of the STARD document http://www.stard-statement.org. Articles presenting novel and reproducible research that introduce new knowledge and observations are especially encouraged. This section also welcomes the submission of topical review papers on relevant subjects.

The *Oral and Maxillofacial Radiology Section* publishes original peer-reviewed contributions to the advancement of diagnostic clinical oral and maxillofacial radiology and related imaging sciences. The section considers original clinical and experimental research papers, technological developments, extensive systematic reviews of the literature, comprehensive pictorial reviews, special reports, and invited papers on subjects that will appeal to clinicians involved in the diagnostic imaging of hard and soft tissue maxillofacial pathology, selection criteria, computer-assisted diagnosis, craniofacial analysis, image-guided surgical navigation, image processing, dosimetry, radiation physics, biology, and safety.
The section also seeks extensive case series representing various expressions of particular conditions, descriptions of innovative imaging technique applications to these series, and description of novel imaging features to assist imaging specialists develop clinical protocols and interpretive knowledge based on multiple observations. Only papers contributing substantively to the body of knowledge in oral and maxillofacial imaging and performed with scientific rigor will be considered. These papers should assist clinicians in developing evidence-based practice and provide improved clinical decision-making regarding the performance of specific techniques and interpretation of resulting images affecting the oral and maxillofacial region. Diagnostic accuracy studies should conform to the principles of the STARD document http://www.stard-statement.org).

Types of Papers

1. Original Research Article. Reports of original research (preclinical, clinical, or translational) that are well-documented, novel, and significant. Original research manuscripts will be organized into six parts: (1) Abstract; (2) Introduction; (3) Materials and Methods; (4) Results; (5) Discussion; (6) References.

2. Review article. Manuscripts that review the current status of a given topic, diagnosis, or treatment. These manuscripts should not be an exhaustive review of the literature but rather should be a review of contemporary thought with respect to the topic. Systematic reviews and meta-analyses manuscripts should follow PRISMA (http://www.prisma-statement.org) and the Institute of Medicines' guidelines (http://www.iom.edu/Reports/2011/Finding-What-Works-in-Health-Care-Standards-for-Systematic-Reviews/

3. Clinicopathologic Conference (CPC). Manuscripts that document interesting, challenging, or unusual cases that present unexpected or interesting diagnostic challenges. The presentation should simulate clinical work-up, including the formulation of a detailed and well thought out differential diagnosis. The complete diagnostic evaluation, management, and follow-up must be included. CPC articles must be organized into six parts: (1) Title: Provide a descriptive clinical title that does not reveal the final diagnosis. (2) Clinical presentation: Describe the clinical and imaging characteristics of the lesion. Use clinical photographs and radiographs as appropriate. (3) Differential diagnosis: List and discuss lesions to be considered as reasonable diagnostic possibilities. The authors are reminded that the most important part of the CPC manuscript is the clinical differential diagnosis, where the authors guide the readership through their own diagnostic thought process. This will require the formulation of a list of the most probable diagnostic possibilities (ideally at least 5-6 entities) based on the clinical presentation, medical history, and/or radiographic studies. (4) Diagnosis: Histopathologic findings illustrated with appropriate photomicrographs. (5) Management: Describe the treatment of the patient and response to treatment. (6) Discussion: Concentrate on the most interesting aspect(s) of the case. No abstract is needed for CPC manuscripts. Limit the number of references to no more than 25.

4. Medical Management and Pharmacology Update (MMPU). This section is intended to provide concise, current reviews of medical problems and how they relate to dentistry. Manuscripts should include a good review of the clinical aspects of the disease, stressing the impact of the disease on the dental management and dental treatment of the patient. Emphasis should be placed on new developments, new research, or new approaches to therapy or management. Manuscripts should not be an exhaustive review of the literature but rather a review of contemporary thought with respect to the topic. Likewise, the bibliography need not be all inclusive but rather should include only seminal, contemporary references deemed by the author to be most pertinent. The desired format for manuscripts submitted for the MMPU section includes: (1) abstract; (2) topic introduction/overview; (3) epidemiology/demographics; (4) etiology and pathogenesis; (5) clinical presentation/physical findings; (6) diagnosis (laboratory tests, diagnostic imaging, etc.); (7) medical management and treatment; (8) complications; (9) prognosis; oral manifestations/dental implications and significance; and (10) dental management (of patients with the disease). Manuscripts should not exceed 12 pages in 12-point, double-spaced Times New Roman (tables and figures count toward the 12-page limit).

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[dataset] 5. Oguro, M, Imahiro, S, Saito, S, Nakashizuka, T. Mortality data for Japanese oak wilt disease and surrounding forest compositions, Mendeley Data, v1; 2015. http://dx.doi.org/10.17632/xwj98nb39r.1.

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