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Doutorado

Assistência mediada por tecnologia: uma abordagem possível em tempos de pandemia?

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Assistência mediada por tecnologia: uma abordagem possível em tempos de pandemia?

Defesa apresentada ao Programa de Pós-Graduação em Odontologia da Faculdade de Ciências da Saúde da Universidade de Brasília, como requisito parcial à obtenção do título de Doutor em Odontologia.

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Defesa de Tese apresentada, como requisito parcial para obtenção do grau de Doutor em Odontologia, Programa de Pós-Graduação em Odontologia da Faculdade de Ciências da Saúde da Universidade de Brasília.

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“A tarefa não é tanto ver aquilo que ninguém viu, mas pensar o que ninguém ainda pensou sobre aquilo que todo mundo vê”.

(Arthur Schopenhauer)

RESUMO

Introdução: O surgimento do novo coronavírus (SARS-CoV-2) resultou em uma crise global de saúde pública (pandemia de COVID-19) Nesse contexto de pandemia, tornou-se fundamental garantir atendimento aos pacientes com câncer, apesar do lockdown e das restrições. A assistência não presencial, mediada por tecnologia, foi uma das alternativas encontradas e se configurou numa abordagem possível.
Objetivos: Avaliar o papel da teleodontologia em pacientes com câncer bucal durante a pandemia de COVID-19 por meio de revisão integrativa da literatura; avaliar a viabilidade da telessaúde no monitoramento de pacientes com câncer de cabeça e pescoço, por meio de revisão sistemática sobre tecnologia remota, adesão do usuário, satisfação do usuário e qualidade de vida e avaliar o uso de ferramentas de inteligência artificial na detecção do câncer comparado aos métodos tradicionais de diagnóstico por imagem por meio de um panorama das revisões sistemáticas.
Metodologia: Foram realizadas uma revisão integrativa, uma revisão sistemática de intervenção e outra revisão sistemática de diagnóstico. A estratégia PICO (População, Intervenção, Comparação e Desfecho) e PIRD (Participante, Teste Índice, Teste de Referência e Diagnóstico de interesse) foram utilizadas. As bases pesquisadas foram PubMed, Cochrane Central Register of Controlled Studies (Cochrane), SciVerse Scopus (Scopus), Web of Science, Latin American and Caribbean Health Sciences (LILACS), Excerpta Medical Database (Embase), Scientific Electronic Library Online (Scielo), Business Source Complete (EBSCOhost) e na literatura cinzenta através do PROQUEST, Google Scholar e JSTOR. Os descritores do Medical Subject Headings (MeSH) foram empregados e foi utilizado o software gerenciador de referências online Rayyan QCRI (https://rayyan.qcri.org/welcome) para remoção de duplicatas, além da remoção manual. Os principais desfechos primários considerados foram os benefícios do uso da TO para pacientes em tratamento de câncer de boca e cabeça e pescoço durante a pandemia de COVID-19; modelo de aplicativo já utilizados em TM/Telesaúde; número de pacientes que aderem ao uso, qualidade de vida e satisfação do paciente no uso do aplicativo de TM/Telesaúde e detecção de cancer e diagnóstico por meio de inteligência artificial. A verificação da qualidade metodológica em estudos individuais foi avaliada pela Lista de Verificação de Avaliação Crítica do *Joanna Briggs Institute* (Instituto Joanna Briggs, 2014).
Resultados: Observou-se que 78% dos pacientes atualmente preferem a teleodontologia; 92% dos pacientes recomendariam o uso da videoconsulta a outros pacientes. A continuidade do atendimento odontológico, a redução de visitas de pacientes ao hospital, a redução do risco de infecção pelo coronavírus e a limitação de consultas presenciais para proteger os profissionais de saúde são benefícios que reforçam o uso da teleodontologia pelas instituições de saúde. Embora tenha havido heterogeneidade quanto à tecnologia utilizada, o monitoramento remoto e/ou autogerenciamento dos sintomas por meio de aplicativos móveis foi viável para a maioria dos pacientes, com graus satisfatórios de aceitabilidade, satisfação, usabilidade e adesão. Fica demonstrado que as várias abordagens de Inteligência

Artificial são promissoras em termos de especificidade, sensibilidade e precisão diagnóstica na detecção e diagnóstico de tumores malignos.
Conclusão: A partir dos artigos realizados, concluiu-se que a Assistência Mediada por Tecnologia, durante a pandemia do COVID 19, nos campos médicos ou odontológicos, como ferramenta para monitoramento remoto de pacientes com câncer de boca e câncer de cabeça e pescoço, foi bem aceita pelos pacientes, e contribuiu para continuidade do atendimento odontológico, para redução das visitas dos pacientes ao hospital, redução do risco de infecção pelo coronavírus e a limitação do atendimento presencial para proteger profissionais de saúde. Todavia, observou-se a necessidade de uma interface mais amigável, de uma avaliação adequada da experiência do usuário para uma concreta aplicabilidade dessas ferramentas para monitoramento de pacientes com câncer de cabeça e pescoço. Nesse contexto, a detecção e diagnóstico de tumores malignos com o auxílio de IA parecem ser viáveis e precisas com o uso de diferentes tecnologias, algoritmos de aprendizado profundo e de máquina e análise radiômica. As revisões realizadas apontam benefícios da assistência mediada por tecnologia também para o cuidado de pacientes com câncer, embora essas tecnologias não sejam capazes de substituir o profissional radiologista na análise de imagens médicas ou odontológicas**.** De maneira que, ainda que as evidências apontem que a assistência mediada por tecnologia foi uma abordagem possível em tempos de pandemia, mais estudos longitudinais multicêntricos são necessários para uma melhor possibilidade de aplicação clínica.

Palavras-chaves: COVID-19, Teleodontologia, Telemedicina, Telessaúde, Monitoramento, Câncer Bucal, Câncer de Cabeça e Pescoço, Inteligência Artificial, Algoritmo, Revisão Integrativa. Revisão Sistemática, Overview.

ABSTRACT

Introduction: The emergence of the new coronavirus (SARS-CoV-2) has resulted in a global public health crisis (COVID-19 pandemic). In this pandemic context, it has become essential to ensure care for cancer patients, despite Lockdown and restrictions. The non-face-to-face assistance, mediated by technology, was one of the alternatives found and was configured in a possible approach.
Objectives: To evaluate the role of teledentistry in patients with oral cancer during the COVID-19 pandemic through an integrative review of the literature; to evaluate the feasibility of telehealth in the monitoring of patients with head and neck cancer through systematic review of remote technology, user adherence, user satisfaction and quality of life and to evaluate the use of artificial intelligence tools in cancer detection compared to traditional methods of diagnostic imaging through a panorama of systematic reviews.
Methodology: An integrative review, a systematic review of intervention and another systematic review of diagnosis were performed. The strategy PICO (Population, Intervention, Comparison and Outcome) and PIRD (Participant, Index Test, Reference Test and Diagnosis of interest) were used. PubMed, Cochrane Central Register of Controlled Studies (Cochrane), SciVerse Scopus (Scopus), Web of Science, Latin American and Caribbean Health Sciences (LILACS), Excerpta Medical Database (Embase), Scientific Electronic Library Online (Scielo)Business Source Complete (EBSCOhost) and in grey literature through PROQUEST, Google Scholar and JSTOR. The descriptors of the Medical Subject Headings (MeSH) were employed and the online reference manager software Rayyan QCRI (https://rayyan.qcri.org/welcome) was used to remove duplicates, in addition to manual removal. The main primary outcomes considered were the benefits of the use of OT for patients undergoing treatment of mouth and head and neck cancer during the COVID-19 pandemic; application model already used in TM/Telehealth; number of patients who adhere to the use, quality of life and patient satisfaction in the use of the TM/Telehealth application and detection of cancer and diagnosis through artificial intelligence. The verification of methodological quality in individual studies was evaluated by the Critical Evaluation Checklist of the Joanna Briggs Institute (Instituto Joanna Briggs, 2014).
Results: It was observed that 78% of patients currently prefer teledentistry; 92% of patients would recommend the use of videoconsultation to other patients. The continuity of dental care, the reduction of visits of patients to the hospital, Reducing the risk of coronavirus infection and limiting face-to-face consultations to protect health professionals are benefits that reinforce the use of teledentistry by health institutions. Although there was heterogeneity regarding the technology used, remote monitoring and/or self-management of symptoms through mobile applications was feasible for most patients, with satisfactory degrees of acceptability, satisfaction, usability and adherence. It is demonstrated that the various approaches of Artificial Intelligence are promising in terms of specificity, sensitivity and diagnostic accuracy in the detection and diagnosis of malignant tumors.
Conclusion: From the articles, it was concluded that Technology-Mediated Assistance, during the COVID 19 pandemic, in the medical or dental fields, as a tool for

remote monitoring of patients with oral cancer and head and neck cancer, was well accepted by patients, and contributed to the continuity of dental care, to reduce patient visits to the hospital, reducing the risk of coronavirus infection and limiting face-to-face care to protect health professionals. However, there was a need for a more user-friendly interface, an adequate evaluation of the user experience for a concrete applicability of these tools for monitoring patients with head and neck cancer. In this context, the detection and diagnosis of malignant tumors with the aid of AI seems to be feasible and accurate with the use of different technologies, deep learning and machine algorithms and radiomic analysis. The reviews indicate the benefits of technology-mediated care also for cancer patients, although these technologies are not able to replace the professional radiologist in the analysis of medical or dental images. Thus, although the evidence points out that technology-mediated care was a possible approach in times of pandemic, more longitudinal multicenter studies are needed for a better possibility of clinical application.

Keywords: Covid-19, Teledentistry, Telemedicine, Telehealth, Monitoring, Oral Cancer, Head and Neck Cancer, Artificial Intelligence, Algorithm, Integrative Review, Systematic Review, Overview.

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LISTA DE ABREVIATURAS E SIGLAS

AI – Artificial Intelligence;
ANN – *Artificial Neural Networks;*
AMLwvf – Angiomiolipoma sem Gordura Visível
AUC – Area Under the Curve;
BMR – Biópsia de Massa Renal;
BUS – Breast Ultrasound;
CADe – Computer-Aided-Detection;
CADx – Diagnostic CAD;
CCP – *Câncer De Cabeça E Pescoço*;
CaCR – *Carcinoma De Células Renais*;
CDR – CAD On Cancer Detection Rate;
CG – Central gland;
CM – Cancêr de Mama;
CO – *Câncer Oral;*
Cochrane – Cochrane Central Register of Controlled Studies;
CCR – *Câncer Colorretal;*
csPCa – D*iagnosing prostate cancer;*
CT – Computed Tomography;
DL – *Deep Learning;*
DNN – Deep Neural Network;
DOPMs – *Doenças Orais Potencialmente Malignas;*
DOR – Diagnostic odds ratio;
DR – Double Reading;
DT – *Decision Tree;*
DTL – Deep Transfer Learning;
EBSCOhost – Business Source Complete;
ECO – *Exame Clínico Oral;*
Embase – Excerpta Medical Database;
EN – Elastic Net;
EORTC QLQ-H&N35 – European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 and Head and Neck Module;
EUA – *Estados Unidos da América;*
EuroQoL – EQ-5D Questionnaire;
EWB – Emotional Well-Being;
FACT-HN – The Functional Assessment of Cancer Therapy-Head & Neck Scale;
HeNeA – *Head And Neck Application;*
HNC – Head Neck Cancer;
HNSCC – Head and Neck Squamous Cell Carcinoma;
HRQOL – Health-Related Quality Of Life;
IRCCS – Istituto Di Ricovero E Cura A Carattere Scientifico;
KNN – *K-Nearest Neighbor;*
LAS/SO – Least Absolute Shrinkage and Selection Operator;
LCT – Lung Conputered Tomography;
LDA – Linear Discriminant Analysis;
LILACS – Latin American and Caribbean Health Sciences;
LIR – Linear regression;
LMS – Learning Management System;
LOR – Logistic regression;

LVQ – Learning Vector Quantization;
MeMoSA – *Mobile Mouth Screening Anywhere;*
MeSH – Medical Subject Headings;
MJA – My Journey Ahead;
MM – Mammography;
MRI – Magnetic Resonance Imaging;
MRONJ – Medication-Related Osteonecrosis Of The Jaw;
NB – *Naive Bayes;*
NPS – Net Promoter Score;
OC – Oral Cancer;
OPMD – Oral Potentially Malignant Disorders;
OR – *Oncocitomas Renais*;
Pca – Prostate Cancer;
PCI-HN – Patient Concerns Inventory – Head and Neck;
PET – Positron Emission Tomography;
PPE – Personal Protective Equipment;
PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses;
PROQUEST – International Prospective Register of Ongoing Systematic Reviews;
PUBMED – *Serviço da Biblioteca Nacional de Medina dos Estados Unidos para acesso gratuito ao Medline;*
PVP-I – Povidone-Iodine;
PWB – Physical Well-Being;
PZ – Peripheral Zone;
QOL – Quality Of Life;
QV – *Qualidade De Vida;*
RES – *Registro Eletrônico De Saúde;*
RF – Random Forest;
RML – Radiomic Machine Learning;
RMSE – Root Mean Squared Error;
RR – Recall Rate;
RS – *Revisão sistemática;*
SARS-CoV-2 – Severe acute respiratory syndrome coronavirus 2;
Scielo – Scientific Eletronic Library Online;
SCOPUS - SciVerse Scopus;
SR – Single Reading;
STT/SC – Telemedicine and Telehealth System;
SVM – *Super/Support Vector Machine*;
SWB – Social Well-Being;
TM – *Telemedicina;*
TO – *Teleodontologia;*
TZ – Transitional Zone;

Sumário

CAPÍTULO 1 - ASSISTÊNCIA MEDIADA POR TECNOLOGIA: A TELEODONTOLOGIA NA LINHA DE CUIDADO DO CÂNCER ORAL E DE CÂNCER DE CABEÇA E PESCOÇO

1.1 INTRODUÇÃO

A rede, o compartilhamento de informações digitais sobre odontologia e as consultas, exames e análises à distância são realizados por um ramo específico da Telemedicina (TM) relacionada à odontologia conhecida como teleodontologia (TO) [1,2]. Nos últimos anos, a área odontológica tem se beneficiado de inúmeras inovações tecnológicas, assim como a medicina e outros setores da saúde. Entre os mais importantes desses avanços na odontologia estão o uso de computadores, tecnologia de telecomunicações, serviços de diagnóstico por imagem digital e hardware e software especializados para triagem e acompanhamento de pacientes [3]. Inovações tecnológicas que eram consideradas implausíveis algumas décadas atrás agora são possíveis na assistência odontológica, mas implementá-las e avaliá-las requer o envolvimento ativo das principais partes interessadas da organização e de especialistas clínicos, tecnológicos e científicos [4]. As novas tecnologias de informação não apenas melhoraram a qualidade do tratamento odontológico do paciente, mas também possibilitaram alcançar resultados parciais ou completo do gerenciamento remoto, mesmo a milhares de kilômetros de distância de centros de treinamento de saúde comunitários ou especializados em odontologia.

A TO não é um conceito novo e um dos primeiros projetos de TO foi iniciado pelos militares dos EUA, em 1994, para servir às tropas dos EUA em todo o mundo [5]. É considerada um domínio da TM especificamente dedicado à odontologia e surgiu da combinação da tecnologia digital e de telecomunicações com a odontologia [6,7]. As implicações da TO para os serviços de saúde bucal tanto em áreas urbanas como em áreas rurais ou remotas são significativas [8]. Possui o

potencial de identificar populações de alto risco, facilitar o encaminhamento dos pacientes a um profissional odontólogo e apoiar o tratamento local, reduzindo assim as listas de espera e viagens desnecessárias e perda de produtividade [5,9-11]. Algumas áreas da odontologia que são particularmente apropriadas para a TO são consultas remotas para preparar planos de tratamento, fornecer cuidados preventivos e supervisionar profissionais que trabalham em ambientes rurais, bem como educação continuada [12]. Nesse cenário, em 2002, a *National Health System* relatou preocupação com o atendimento odontológico de pacientes que viviam em regiões remotas e isoladas, declarando ser a TO uma alternativa de suporte para dentistas que atuavam nessas regiões [13], apresentando-se também como uma maneira mais acessível de fornecer serviços à população [11], especialmente em tempos difíceis como no período da pandemia Covid-19.

O mundo já passou por algumas epidemias e pandemias. Alguns exemplos são a pandemia de 1918-1920 (Gripe Espanhola), 1957-1958 (Gripe asiática H2N2), 1968-1969 (Gripe de Hong Kong H3N2), 1977-1978 (Gripe russa H1N1), 1997-2004 (Gripe Aviária H5N1) e 2009 (Gripe Suína H1N1). A pandemia de COVID-19 se apresentou como uma infecção viral agressiva que se espalhou pelo mundo de outubro de 2019 até maio de 2023. É difícil saber quando, como e de que será a próxima pandemia. O que se pode ter certeza é da inevitabilidade da ameaça de uma provável nova pandemia. Estar preparado para um amplo espectro de situações pode ajudar a enfrentá-la. Um dos aspectos interessantes dessa preparação abrange muitos dos recursos necessários para fazer frente a uma epidemia, como, acesso adequado a cuidados e tratamentos médicos; existência de um número adequado de profissionais de saúde qualificados que possam detectar surtos suspeitos; laboratórios equipados com a capacidade de diagnosticar patógenos emergentes; sistemas de informação que conectem em tempo real clínicas e laboratórios com a rede de saúde pública; quantidade suficiente de suprimentos médicos, inclusive equipamento de proteção individual (como máscaras e luvas); e uma comunicação eficaz com a comunidade e sua participação e colaboração nas medidas a serem adotadas. Em resumo, trata-se de melhorar os sistemas de vigilância, notificação, investigação e resposta. [14].

O aprendizado deixado pela pandemia de COVID-19 é que ficou claro a importância de contar com infraestrutura científica. No Brasil, se não fossem os

laboratórios estruturados como da USP, Unesp, Unicamp, Unifesp e de todas as instituições que atuam com pesquisa, não teria sido possível implementar um sistema capaz de fazer diagnósticos tão rapidamente. Outros aprendizados importantes consistem na valorização da ação de equipes de saúde multidisciplinares; otimização do gerenciamento da quantidade de dados gerados pela volume crescente de exames de laboratórios, com a automatização e realização de processos de trabalho de forma online e remota; e estruturação de laboratórios de contenção do tipo NB3 para lidar com vírus, bactérias e outros microrganismos que são classificados como perigosos demais para serem estudados nos laboratórios de tipo NB2 [15].

À medida que o coronavirus se espalhou por gotículas, fômites e transmissão de contato, a interação face a face do profissional de saúde com o paciente apresentou o risco de sua transmissão. Como o tratamento odontológico invariavelmente envolve inspeção cuidadosa, exame, intervenções diagnósticas e terapêuticas da região naso-orofaríngea, os profissionais de odontologia são suscetíveis a serem infectados pelo coronavírus [16]. Com o surto da *Severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2), serviços odontológicos eletivos e não essenciais foram suspensos em muitos países para conter a disseminação comunitária do vírus[17-18]. Isso, mais do que nunca, destacou a necessidade de estratégias alternativas para facilitar a continuidade dos cuidados [19].

Especificamente, a via de transmissão desse coronavírus tem um envolvimento significativo da prática odontológica. Muitos procedimentos odontológicos produzem aerossóis e gotículas contaminadas por microrganismos que facilitam a disseminação de infecções [20]. A TO pode ser incorporada à prática odontológica de rotina, pois oferece uma ampla gama de aplicações, como triagem remota de pacientes suspeitos de Covid-19 para tratamento odontológico e diminuição da exposição desnecessária de pacientes saudáveis ou não infectados ao diminuir suas visitas a consultórios odontológicos já sobrecarregados e hospitais [21]. Cabe salientar que outros tipos de pacientes como acamados, portadores de deficiência, imunodeprimidos, em tratamento radioterápico/quimioterápico também podem se beneficiar desse tipo de atendimento remoto quanto a melhoria da sua qualidade de vida (QV), evitando sua exposição a um ambiente contaminado.

No tocante ao telemonitoramento, este se apresenta como uma subdivisão da TO, que se compõe da teleconsulta, da telediagnose e da teletriagem [21]. O monitoramento de pacientes odontológicos requer visitas frequentes dos pacientes ao dentista para monitorar o progresso do tratamento [22].

O uso de telemonitoramento pode substituir as visitas físicas frequentes por visitas virtuais para monitoramento regular dos resultados do tratamento e progressão da doença [23]. Em estudos durante esta pandemia, o telemonitoramento pareceu ser uma ferramenta promissora no monitoramento remoto de pacientes odontológicos cirúrgicos e não cirúrgicos, especialmente reduzindo custos e tempos de espera [23-25].

A TM é um subconjunto da telessaúde que utiliza de redes de comunicação para prestação de serviços de saúde e de educação médica de uma localização geográfica para outra, principalmente para enfrentar desafios como distribuição desigual e escassez de infraestrutura e de recursos humanos [26]. A TM modificou completamente a abordagem médica tradicional de trabalho, promovendo um método virtual de visitas, consultas e acompanhamento em vez do contato físico e avaliações clínicas presenciais [27]. As vantagens mais significativas da TM são: (1) consulta em tempo real e (2) armazenamento e envio de dados; no entanto, a TM não está livre de desvantagens, incluindo a troca de informações sensíveis, o compromisso com a confidencialidade, o compromisso com a segurança e um grande volume de dados armazenados [28], percepção de que a consulta à distância pode ser menos precisa devido à falta de exame físico [29] e muitos projetos permanecem no ambiente de pesquisa ou como pilotos e não conseguem ser integrados aos caminhos clínicos, devido a barreiras administrativas, regulatórias e de infraestrutura [30] .

No tocante que a patologia oral deve ser baseada no exame clínico, na cavidade bucal em particular, a TM permite distinguir lesões potencialmente malignas das realmente malignas que exige uma abordagem imediata, sem a presunção de fazer um telediagnóstico preciso [31,32]. Percebe-se a capacidade de controlar pacientes com lesões potencialmente malignas, osteonecrose da mandíbula relacionada a medicamentos e doenças auto-imunes, comparando as fotos recebidas com as últimas fotos tiradas na clínica odontológica. Para lesões potencialmente malignas, quaisquer modificações clínicas podem ser avaliadas para

determinar o risco de transformação maligna. Além disso, as doenças auto-imunes requerem o manejo de possíveis recorrências, dor e limitações funcionais orais [33,34]. Para osteonecrose da mandíbula relacionada a medicamentos, sequestro ósseo, possível superinfecção e dor podem ser avaliados para controlar a estabilidade ou piora das lesões [35-37]. Pacientes que vivem em diferentes partes de uma cidade, de um país ou em outros países onde restrições severas foram adotadas para fortalecer a contenção de COVID-19 podem se beneficiar dessa tecnologia. Sem a digitalização e a conversa online, o isolamento social imposto não teria permitido o acompanhamento do seu desenvolvimento clínico[38].

Quanto ao tratamento oncológico, houve à interrupção da prestação de cuidados odontológicos a todos os pacientes, para os quais é indispensável, devido a pandemia de COVID-19. Embora as consultas presenciais sejam reduzidas durante a pandemia, a TO pode atuar como um meio para evitar a interrupção do atendimento através do fornecimento de suporte aos pacientes submetidos a rádio e/ou quimioterapia por telefone e, quando possível, por video-chamadas [39], motivação e ênfase as medidas de higiene oral. Os pacientes que vão se submeter a oncoterapia devem ser informados sobre o que esperar durante o tratamento oncológico (como mucosite, xerostomia e possível disgeusia) e as ações que podem ser tomadas para atenuar esses efeitos [40]. Os pacientes devem ser aconselhados sobre a necessidade de melhorar a higienização dos dentes antes que as manobras de higiene oral se tornem difíceis de manter devido ao desconforto e à necessidade de impedir o risco de cárie que surge devido à hiposalivação, consumo exgerado de caboidratos fermentaveis e a deficiênca no uso de deintifricios com alto teor de fluor. A importância do acompanhamento em longo prazo também precisa ser discutida, especialmente no que diz respeito a cáries e osteorradionecrose [41]. Em caso de algum sintoma, o dentista pode solicitar fotografias ou radiografias, se necessário, para auxiliar no diagnóstico e aconselhar medidas de atendimento domiciliar, quando viável [39]. Podem ser realizados check-ups constantes, aconselhamento e apoio por meio de consultas de TO, para manter e melhorar o bem-estar geral dos pacientes e, consequentemente, a QV.

Entretanto, muitos são os desafios na padronização da TO. Entre os desafios elencados pelos odontólogos estão a falta de aceitação da TO pelos cirurgiões-dentistas, que pode ser atribuída à complexidade da TO e resistência ao

aprendizado de novas habilidades [30,42], medo de fazer um diagnóstico impreciso, preocupação com o aumento de custos e despesas, restrições relacionadas à infraestrutura, como acesso precário à Internet, falta de hardware, falta de treinamento, falta de suporte técnico e especialização, incompatibilidade organizacional da TO com o sistema de saúde, reembolso financeiro insuficiente, orientações inadequadas, descoordenação entre centro remoto e a ponta final e alto custo de instalação [30], a representação bidimensional das lesões e a incapacidade de realizar testes como palpação e ausculta [43].

Os sistemas disponíveis para a execução da TM e/ou TO ainda são restritos, mas representam uma ferramenta fácil, viável e acessível, útil tanto para profissionais de saúde quanto para pacientes [44,45]. Essa comunicação pode ocorrer por meio de aplicativos de mensagens instantâneas (*WhatsApp, Telegram, Instagram, SMS, Messenger*) e aplicativos de video-chamada (*Google Meet, Skype, Facetime, WhatsApp*). Um estudo publicado por Petruzzi et al. [45] confirmou a utilização do WhatsApp como suporte no diagnóstico oral, em que 82% dos casos teleconsultados concordaram com o diagnóstico clínico-patológico, sugerindo que é uma boa opção para a TO.

É importante ressaltar que o uso de aplicativos e softwares na odontologia vai além do gerenciamento do processo saúde-doença e também contribui para o ensino e aprimoramento das capacidades dos recursos humanos. O desenvolvimento de soluções inovadoras para maximizar a aprendizagem acelerou com a chegada da pandemia de COVID-19. A fim de garantir a continuidade do semestre de instrução, tornou-se necessário a transição de métodos de aprendizagem presencial para métodos de aprendizagem online. Isso foi feito por meio de soluções tecnológicas como *Zoom* e *Slack* (ambos da Slack Technologies, San Francisco, Califórnia) [46], bem como pela implementação de novos protocolos de práticas clínicas destinados a proteger a saúde de professores, alunos, funcionários e pacientes [47]. Nesse contexto, as plataformas virtuais de aprendizagem com programas bem elaborados têm potencial para desempenhar um papel significativo e útil [48].

Mobile learning é o uso de tecnologia em dispositivos móveis para educação (m-learning) [49]. Os resultados da pesquisa de aprendizagem móvel enfatizam que esta tecnologia pode levar a uma aprendizagem mais significativa quando os

materiais de aprendizagem são projetados adequadamente de acordo com as necessidades e interesses dos alunos [50] Portanto, há vantagens na aprendizagem móvel em comparação com a educação tradicional. São inúmeros os métodos de ensino utilizados em programas educacionais que fazem uso da Internet. Em outras palavras, ao entender quais tipos de ferramentas e padrões de uso os alunos já possuem em seus próprios smartphones, é possível projetar atividades educacionais de acordo e oferecer a eles oportunidades de educação igualitária.

A otimização de softwares e procedimentos, tanto para o gerenciamento do processo saúde-doença como para o ensino e aprendizado em odontologia, levaria a um melhor manejo dos pacientes e uma alternativa de ensino. Embora a tecnologia seja de grande suporte no manejo de pacientes, principalmente em períodos de emergência, ela não está isenta de desvantagens como custos, segurança e implicações para o sigilo dos dados [51]. Dessa forma, o desenvolvimento de aplicativos voltados para o monitoramento de lesões bucais apresentados por meio de projetos de simulação especifica gera o cuidado na área de oncologia e eficácia no controle de manifestações bucais do tratamento oncológico, dando tranquilidade ao paciente e prevenindo o agravamento do quadro geral paciente.

Quanto à legislação sobre o tema, a Lei nº 5.081 de 24 de agosto de 1966, que regula o exercício da Odontologia no Brasil, perpassa, na alínea Artigo 7, o registro que "é vedado ao cirurgião-dentista consultas mediante correspondência, rádio, televisão, ou meios semelhantes". Essa circunstância trouxe, ao exercício da TO, um espaço de argumentações conflitantes, apesar dos benefícios observados durante a pandemia por covid-19 em 2020. Uma primeira tentativa de regulamentação do CFO ocorreu na Resolução nº 92 de 2009. Entretanto, a resolução nº 92 foi revogada pela Resolução 227/2020. Em 2020, também foi publicada a Resolução 226/2020, na qual "fica expressamente vedado o exercício da Odontologia a distância, mediado por tecnologias, para fins de consulta, diagnóstico, prescrição e elaboração de plano de tratamento odontológico" [52].

Com o debate sobre o crescimento tecnológico e a ciência da TO, sendo edificada no contexto mundial e adquirindo robustez e relevância na pandemia de 2020, a Resolução 228/2020, publicada na sequência das anteriores, faz um

delineamento relevante para a aplicação da Odontologia a distância no âmbito do SUS, porém com restrição ao período de pandemia. Atualmente o Ministério da Saúde trabalha em conjunto com o Conselho Federal de Odontologia para incorporar o uso da TO de forma permanente no SUS [52].

1.2 REVISÃO DE LITERATURA

Em Wuhan, na China, em dezembro de 2019, houve um aumento incomum de casos de pneumonia. A Organização Mundial de Saúde renomeou o fator etiológico, um novo coronavírus, como "doença de coronavirus SARS-CoV-2" (Covid-19).

A rápida disseminação da Covid-19 pelo mundo e na China levou à definição dessa condição patológica como uma pandemia. A Itália se tornou uma das primeiras nações da Europa a ser gravemente afetada, com um número crescente de pacientes infectados. Nesta situação de emergência, novos modelos de atendimento foram incentivados, restringindo a comunicação direta entre o médico e o paciente. Aconselhou-se evitar hospitais, consultórios odontológicos e outros consultórios médicos sempre que possível, pois os estabelecimentos de saúde apresentavam maior risco de infecção cruzada [3]. Passou-se a lavar as mãos com água e sabão e limpar e desinfetar objetos e superfícies tocados com frequência, cobrir a boca e o nariz ao tossir ou espirrar com o uso constante de máscaras ao andar pelas ruas e ambientes fechados, ficar em casa quando estiver doente, sendo o isolamento social umas das principais medidas preventivas durante o período de grave disseminação.

A pandemia da Covid-19 deixou um legado quanto às ações de saúde com diversos ensinamentos. Deixou claro que é preciso investir mais em saúde pública e em saneamento básico, e que o sistema de saúde privado precisa estar integrado ao sistema público de saúde, no tocante a disponibilização de leitos, formação de recursos humanos, acesso às ações preventivas e assistenciais no combate a disseminação de agentes infecciosos, assessoria técnica para produção de respiradores, compra de EPI´s para hospitais públicos, dentre outras ações. Além

disso, ficou claro a mudança político-social que a pandemia de Covid-19 gerou na população em escala global, como a ampliação do trabalho remoto, as alterações na mobilidade urbana e nas relações de trabalho, o incremento da precarização na vida dos trabalhadores, acirramento das disputas entre liberais, populistas e ex-socialistas que se confrontam entre as resistências democráticas e as ameaças autoritárias, em busca de saídas para a crise global que nem sempre são afinadas com os interesses históricos da classe trabalhadora [53].

Muitos procedimentos cirúrgicos odontológicos resultavam na produção de aerossóis e seringas que eram contaminadas com microrganismos que promoviam a disseminação de infecções [4].

Tecnologias de comunicação como smartphones, tablets e laptops apoiaram o rápido desenvolvimento da TM como uma nova ideia na assistência médica para fornecer atendimento remoto [5]. A TM alterou completamente a abordagem médica tradicional de trabalho, promovendo um método virtual de visitas, consultas e acompanhamento no lugar do contato físico e avaliações clínicas presenciais.

A pandemia de Covid-19 criou desafios sem outros meios de garantir os cuidados de saúde. No entanto, o uso potencial de sistemas e métodos de telessaúde em odontologia, também conhecidos como TO, podiam melhorar o calibre e a eficácia da assistência odontológica [8].

Várias pesquisas foram realizadas visando estabelecer a relação da TM/TO, através de aplicativos, no monitoramento de pacientes com câncer oral e de cabeça e pescoço, assim como no uso de inteligência artificial na detecção de câncer em paralelo com os métodos tradicionais de imagem médicas.

1.2.1 **Associação entre a Aplicativos de Telemedicina/Teleodontologia com o Monitoramento de Pacientes com Câncer Oral e de Cabeça e Pescoço**

Em 11 de março de 2020, a Organização Mundial da Saúde declarou a doença de coronavírus 2019 (COVID-19) uma pandemia. Desde então, a área médica viu uma mudança radical na forma como o atendimento ao paciente é prestado, com muitas consultas ambulatoriais não urgentes sendo canceladas,

reagendadas ou convertida em uma plataforma virtual para diminuir a carga sobre pacientes e funcionários, evitando exposições potenciais desnecessárias ao vírus. Isso resultou em uma expansão rápida e sem precedentes dos serviços de TM em toda a comunidade médica. Embora a TM não seja um conceito novo, até recentemente houve uma adoção lenta devido a várias barreiras, incluindo desafios técnicos, resistência à mudança, reembolso e vários fatores específicos do paciente, como idade, nível de educação e conhecimento de informática. Em relação as barreiras atuais para a TM entre pacientes com câncer de cabeça e pescoço (CCP), a maioria dos pacientes com CCP preferia visitas clínicas presenciais à TM quando podiam escolher. Embora a TM inegavelmente teve suas próprias vantagens durante a fase crítica da pandemia de COVID-19, as preferências do paciente, as barreiras relacionadas à tecnologia e as limitações relacionadas à vigilância virtual do câncer são abordadas para maximizar a eficácia da TM no tratamento do CCP no futuro [54].

Isso se verifica quando se examina a concordância no diagnóstico clínico de lesões de alto risco na cavidade oral e decisões de encaminhamento entre exame clínico oral (ECO) e TO. Há evidências de que a TO pode ser usada para comunicação entre a atenção primária e os especialistas em medicina oral e pode ser facilmente integrada ao ambiente clínico para o manejo do paciente, mostrando que pode ser alcançada uma concordância moderada a alta entre o ECO e o diagnóstico a partir da revisão de imagens [55].

Os mesmos aspectos são observados na avaliação dos benefícios da integração da TO nos serviços de saúde de rotina, através de uma visão geral das evidências da eficácia e do impacto econômico da TO. Há evidências emergentes que apoiam a eficácia da TO e a análise econômica referindo-se à minimização de custos, de forma que o uso da teleconsulta em odontologia pode ser econômico quando comparado a uma consulta convencional. No entanto, estudos econômicos de alta qualidade em TO são raros. Assim, ainda não há evidências conclusivas suficientes, particularmente quanto à sua eficácia, custo-efetividade e uso a longo prazo, para tomar decisões políticas baseadas em evidências em TO [2].

O câncer oral (CO) continua entre os dez tipos mais de câncer mais comuns no Brasil, apesar de ser amplamente evitável. O uso generalizado de tecnologia no consultório, combinado com os avanços nos recursos de registro eletrônico de

saúde (RES), apresenta oportunidades para melhorar a triagem do CO por dentistas, especialmente para pacientes desfavorecidos com necessidades graves de saúde. A partir do desenvolvimento de um protocolo para o uso de câmeras intraorais associado a teleorientação que facilita, via RES, a consulta com um especialista em patologia bucal, observa-se a viabilidade e a aceitabilidade na implementação de uma intervenção de teleorientação auxiliada pela detecção e identificação de lesões bucais durante as visitas odontológicas de rotina. A realização de ensaios posteriores maximizará a validade externa do modelo de teleorientação e facilitarão a ampla implementação, disseminação do modelo de ensino de dentistas e residentes, com o objetivo final de melhorar o atendimento ao paciente e utilização sustentada do rastreamento do CO baseado em evidências, orientações de encaminhamento e coordenação do cuidado [56].

Um exemplo é o uso de câmera intraoral com o método combinado de autofluorescência e luz branca LED usada para doenças orais potencialmente malignas (DOPMs) na triagem de CO em TO. A validade e confiabilidade do método combinado para triagem de displasia em DOPMs são superiores quando comparado ao método autofluorescente sozinho. A câmera intraoral com auxílios fluorescentes para triagem de DOPMs pode ser utilizada para triagem via TO [57].

Até 86% dos pacientes com CO apresentam-se em estágio tardio, onde a sobrevida é baixa. O acesso limitado ao diagnóstico especializado é um fator significativo para a apresentação tardia. O uso crescente de smartphones apresenta uma oportunidade de usar a tecnologia digital para facilitar a detecção precoce do CO. Felizmente, o CO é um dos poucos tipos de câncer passíveis de detecção precoce sem a necessidade de equipamentos médicos caros. Uma grande vantagem é que até 80% dos COs se desenvolvem a partir de uma lesão precursora, e a cavidade oral é passível de exame visual, proporcionando uma oportunidade de detectar essas lesões precocemente para intervenção a fim de prevenir a transformação maligna em câncer [58]. Um telefone celular pode ser uma ferramenta sensível e específica na detecção precoce de lesões da mucosa oral, com uma sensibilidade maior de 80% para detectar uma lesão, uma precisão de 87% para categorizar o tipo de lesão e uma concordância de 85% no encaminhamento do paciente entre o exame clínico e o uso de um telefone celular [55].

O uso de aplicativos como o *Mobile Mouth Screening Anywhere* (MeMoSA) é capaz de documentar lesões dentro da cavidade oral, e indivíduos com lesões pré-cancerosas e benignas são identificados por meio de consulta nas funções do aplicativo. Com a implementação em larga escala do MeMoSA, as barreiras logísticas e de acesso que impedem a detecção precoce de CO são abordadas, simplificando o encaminhamento que promove a intervenção precoce e maximiza os recursos de saúde, especialmente em um ambiente de poucos recursos, onde a maioria dos CO são diagnosticados [59]. Há evidências de que a implementação do MeMoSA® como uma ferramenta para facilitar a identificação e encaminhamento preciso de CO e DOPMs é confiável e válida. Isso pode resolver a inacessibilidade dos profissionais de saúde devido à disponibilidade limitada de especialistas em saúde bucal em países de baixa e média renda ou mesmo durante períodos pandêmicos, como na COVID-19, para reduzir o risco para os profissionais de saúde e a exposição desnecessária do paciente [60].

Diante das crescentes demandas dos serviços, o uso de processos de triagem computadorizada tem sido proposto para otimizar a triagem de pacientes e aumentar a eficiência e a sinergia das práticas assistenciais multidisciplinares. O uso de um novo sistema, *ScreenIT*, para detectar o estado de deglutição, nutrição e angústia em pacientes com CCP que recebem quimiorradioterapia, no intuito de facilitar encaminhamentos apropriados para gerenciamento de equipe multidisciplinar, demonstra que o *ScreenIT* identifica os principais sintomas associados à quimiorradioterapia para CCP com níveis clinicamente aceitáveis de precisão para avaliação clínica e valida alta sensibilidade para detectar preocupações e sofrimento relatados pelo paciente. Os caminhos de gerenciamento gerados pelo *ScreenIT* também verificam a capacidade de identificar pacientes que precisam ser encaminhados para membros da equipe multidisciplinar para intervenção de cuidados de suporte. Dessa forma, sistemas de triagem computadorizada fornecem um meio eficaz e eficiente de monitorar o estado funcional relatado pelo paciente durante quimiorradioterapia e permitem a priorização eficaz e intervenção direcionada para deglutição, nutrição e desconforto para pacientes com CCP no futuro [61].

Por conseguinte, a atual escassez de serviços de saúde e o aumento da incidência de câncer destacam a necessidade de novas estratégias para garantir

tratamentos, cuidados e acompanhamento ideais para todos os pacientes. Os cuidados de saúde digitalizados, que englobam vários conceitos (saúde digital, TM, telemonitorização e terapêutica digital), são uma opção promissora para responder as necessidades para pacientes e cuidadores de CCP. Os cuidados de saúde digitalizados permitem a detecção precoce de distúrbios de saúde, melhoram o gerenciamento do paciente, a QV, a autoconfiança e a comunicação. Além disso, a assistência médica digitalizada é significativamente econômica em termos de tempo e custo. Embora os benefícios da saúde digital são relatados como viáveis e clinicamente relevantes, esforços futuros devem se concentrar na demonstração da utilidade clínica em ensaios clínicos bem projetados. Essa abordagem tem o potencial de melhorar o manejo e a QV dos pacientes e mudar a maneira como os pacientes interagem com familiares e profissionais de saúde [62].

1.2.2 O Uso de Inteligência Artificial (Algorítmos) na Detecção de Câncer em Paralelo aos Métodos Tradicionais de Imagem Médicas.

A literatura atual carece de estudos que tratam do uso de ferramentas de AI na detecção e diagnóstico de CO e CCP. Dessa forma, é observado na literatura muitos estudos que trazem o uso dessas ferramentas na detecção e diagnóstico de diversos tipos de câncer. Neste contexto, a prática radiológica depende em grande parte da interpretação subjetiva dos dados de imagem por um radiologista especialista. Os relatórios são, portanto, dependentes da experiência do leitor. Marcadores de imagem quantitativos e independentes do leitor podem complementar a opinião de especialistas e aumentar a precisão diagnóstica, preditiva e prognóstica. A radiômica inclui várias estratégias destinadas a converter imagens médicas em dados quantitativos, mináveis e de alta dimensão. Estes incluem análise de histograma, textura e forma que extraem informações de dados de imagem que podem não ser visíveis ao olho humano. Nos últimos anos, o aumento do interesse no uso de radiômica em imagens oncológicas levou à sua aplicação como uma ferramenta para derivar informações diagnósticas, preditivas e prognósticas de imagens clínicas de rotina. Apesar do uso extensivo em pesquisas e

relatórios que ligam a textura de *Computed Tomography* (CT) e *Magnetic Resonance Imaging* (RMI) à caracterização da lesão, sobrevida e resultado perioperatório em várias malignidades, a tradução para a prática clínica ainda não ocorreu. Um exemplo é a análise da diferenciação de lesões renais benignas, especialmente a oncocitoma e angiomiolipoma sem gordura visível (AMLwvf) do carcinoma de células renais (CaCR) por meio da análise radiômica de CT e RMI. Os modelos radiômicos são promissores para aumentar o diagnóstico radiológico no câncer renal. A diferenciação de AMLwvf e CaCR mostra a capacidade moderada de radiômica para facilitar essa distinção. No entanto, são necessários ensaios radiômicos prospectivos bem projetados e adequadamente desenvolvidos para que esses novos marcadores de imagem demonstrem sua validade e progresso em direção à tradução clínica [63].

Outra abordagem interessante que pode ser utilizada na detecção precoce de tumores é o uso, por exemplo, da análilse radiômica de CT para distinguir CaCRs de oncocitomas renais (OR). Embora a biópsia de massa renal (BMR) seja uma opção de tratamento para massas renais pequenas, é um procedimento invasivo com potencial para complicações. Além disso, a heterogeneidade intratumoral pode afetar a precisão diagnóstica do BMR. Além disso, as abordagens diagnósticas atuais por meio de imagens transversais tradicionais e BMR têm limitações. A radiômica é a análise quantitativa de imagens com base em pixels ou voxels. Há um crescente interesse e utilização da radiômica tanto para a caracterização do tumor (por exemplo, classificação e diferenciação) quanto para a previsão clínica (por exemplo, sobrevida). O uso contemporâneo da radiômica no CaCR tem se concentrado principalmente em aumentar a precisão da subtipagem histológica não invasiva pré-operatória de pequenos tumores renais para melhor informar o gerenciamento. Dada a grande quantidade de recursos extraídos de imagens (por exemplo, forma; intensidade; e relação espacial de voxels), a radiômica é frequentemente combinada com ML ou DL a fim de derivar relações significativas entre características e um resultado clínico relevante. A análise radiômica de CT tem um alto grau de precisão em distinguir CaCRs de OR, incluindo CaCRs cromófobos de OR. Os algoritmos de radiômica têm o potencial de melhorar o diagnóstico em cenários tradicionalmente ambíguos. No entanto, para que essa modalidade seja implementada no cenário clínico, é necessária a padronização dos protocolos de

aquisição e segmentação de imagens, bem como o compartilhamento interinstitucional de software [64].

Outra situação é o uso de radiômica para a previsão do resultado do tratamento e sobrevida em pacientes com câncer colorretal (CCR) por meio de imagens de CT, RMI e *Positron Emission Tomography* (PET). A radiômica no CCR promete prever a resposta ao tratamento e o resultado a longo prazo; em particular, a radiômica baseada em RMI para CCR mostrou o maior potencial. Pesquisas futuras, em CCR, devem se concentrar na validação independente de modelos promissores existentes ou no desenvolvimento de novos modelos para novas questões de pesquisa [65]. Da mesma forma, as aplicações do uso da análise radiômica de CT com contraste, RMI e a PET no diagnóstico do câncer de laringe apresenta um grande potencial para melhorar vários aspectos do tratamento do câncer de laringe, desde o estadiamento, prognóstico até a previsão da resposta ao tratamento, com o intuito da integração da radiômica no tratamento do câncer de laringe. No entanto, a falta de dados exclusivos sobre o câncer de laringe inibe conclusões firmes. Para implementar a radiômica na prática clínica, é necessário um esforço unificado de pesquisa para padronizar a prática radiômica [66].

O câncer de pulmão é a principal causa de morte por câncer no mundo. Nos países desenvolvidos, os pacientes diagnosticados com esta patologia têm uma taxa de sobrevida em cinco anos entre 10 e 16%. No entanto, nos casos em que o câncer de pulmão é diagnosticado em estágios iniciais, a taxa de sobrevida em cinco anos aumenta para 70%. Na prática clínica, o diagnóstico de nódulos pulmonares ainda é feito por radiologistas com base nas informações dos nódulos (textura, intensidade e forma, etc.). Eles precisam analisar um grande número de imagens de CT e diferenciar os nódulos malignos dos benignos de forma eficiente e precisa. No entanto, isso é extremamente subjetivo e desafiador. Devido a fatores desestabilizadores, como má interpretação, experiência e distração, bem como erro de percepção, é difícil para os radiologistas classificar com precisão os nódulos pulmonares benignos e malignos nas imagens de CT [67,68].

Sistemas avançados de detecção e diagnóstico de nódulos pulmonares são necessários para ajudar os radiologistas a superar esses desafios, interpretar os dados de diagnóstico e tomar decisões. Esses sistemas são conhecidos como sistemas de *Computer-Aided-Detection* (CAD). O interesse é fornecer uma visão

abrangente para apresentar as técnicas de ponta, tanto técnicas tradicionais quanto técnicas de *Deep Learning (*DL), usadas para diagnosticar nódulos pulmonares em *CADx systems* com imagens de CT. A vantagem do DL é a capacidade de aprender recursos altamente discriminativos de várias fontes de dados verificados, assim como há uma tendência em desenvolvimento de técnicas de DL usadas para classificação de nódulos que usam dados de entrada 3D para codificar informações espaciais mais ricas de nódulos e a sim desenvolver redes mais profundas ou mais amplas para caracterizar nódulos. A *Area Under the Curve* (AUC) média obtida pelo método baseado em DL é de 0,904, superior à AUC obtida pelo método tradicional, com média de 0,889. O método de DL também possui maior h*igher accuracy* do que o método tradicional (média de 88,31% vs. 87,58%), dessa forma, os métodos baseados em DL surgem como abordagens promissoras para o diagnóstico de nódulos pulmonares, e acredita-se que as técnicas de DL alcançarão um avanço com base em suas vantagens no diagnóstico de câncer de pulmão [67]. Nesse cenário, técnicas automatizadas de processamento de análise de imagens podem ser aplicadas como ferramentas de auxílio médico na tentativa de minimizar essas dificuldades. Os sistemas são conhecidos como CAD *systems* e vão além do processamento de imagens para fornecer informações específicas sobre a lesão que podem auxiliar radiologistas no diagnóstico. Os CAD *systems* e se mostraram úteis para a construção de ferramentas de auxílio ao diagnóstico médico. No entanto, existem alguns aspectos que ainda requerem atenção, como aumentar a sensibilidade do algoritmo, reduzir o número de falsos positivos, melhorar e otimizar a detecção do algoritmo de diferentes tipos de nódulos com tamanhos e formas diferentes e, finalmente, a capacidade de integração com o Sistema Eletrônico Sistemas de registros médicos e sistemas de comunicação e arquivamento de imagens [68].

A incidência de câncer de mama (CM) em mulheres aumentou significativamente nos últimos anos. A experiência do médico em diagnosticar e detectar o CM pode ser auxiliada pelo uso de alguns algoritmos de classificação e extração de recursos computadorizados. É necessário investigar o estado da arte da relação dos CAD para o CM. Esses métodos são de difícil comparação entre si devido a vários fatores. Alguns desses fatores são: os bancos de dados usados para avaliação, as amostras de imagens selecionadas para avaliação, o número de

amostras usadas, a abordagem de avaliação (metodologia de validação, conjunto de treinamento e teste) usada, sendo que o classificador Super Vector Machine (SVM) tem sido amplamente utilizado para fins de classificação do tecido mamário. Em países que utilizam o CAD, rotineiramente na clínica, encontra discordância sobre a viabilidade de seu uso devido a alguns problemas, como aumento de tempo e custo devido a falsos positivos e falta de treinamento que levam a ignorar lesões suspeitas. A observação dessas questões durante a aplicação clínica dos CADs leva à melhoria de seu desempenho, reduzindo assim os falsos positivos que podem acarretar custos psicológicos, físicos e econômicos, e reduzindo as leituras de falsos negativos que podem ocasionar o abandono do tratamento [69].

Protocolos são desenvolvidos no intuito de verificar a hipótese de que o sistema de *Artificial Intelligence* (AI) é preciso na distinção entre doenças benignas e malignas da mama. O interesse é avaliar que ao extrair características morfológicas e de textura de lesões benignas e malignas, a AI pode ajudar os médicos a fazer análises mais detalhadas das imagens e fornecer uma base objetiva para o diagnóstico. Ao mesmo tempo, o sistema de diagnóstico assistido por AI também pode ser usado para diagnóstico por imagem de CM com amplas perspectivas de aplicação, incluindo detecção de lesões de mama, julgamento de benigno e maligno, classificação patológica e previsão de prognóstico, etc., possuindo alta especificidade na diferenciação de lesões mamárias benignas e malignas e podendo se tornar uma importante ferramenta auxiliar no diagnóstico de doenças mamárias [70].

Os CCPs são definidos como tumores que se desenvolvem na região da cabeça e pescoço, que inclui tumores de glândula salivar, faringe, laringe, cavidade oral, cavidade nasal, seios paranasais e tireóide. Atualmente, os CCPs são tratados com radioterapia, quimioterapia, cirurgia ou uma combinação deles. O tumor cerebral é um dos outros tipos de neoplasias que também podem se desenvolver na região de cabeça e pescoço, mas seu diagnóstico e processo de tratamento são diferentes dos CCPs. Os gliomas são o tipo mais comum de tumor cerebral primário em adultos que, com base nos critérios clínicos e na histopatologia, são classificados como I a IV. O grau IV (glioblastoma multiforme) é considerado o tipo mais grave com maior taxa de disseminação. A ressonância magnética é uma técnica de imagem eficaz no processo de diagnóstico de CCPs e tumores cerebrais

devido ao emprego de radiação não ionizante e sua maior resolução de tecidos moles, além do emprego de agentes de contraste, bem como aquisição de imagens diferentes usando vários parâmetros de imagem. É a modalidade de imagem comumente usada para avaliar CCPs e tumores cerebrais em contraste com outros procedimentos de imagem, incluindo PET e CT. Para detectar CCPs e tumores cerebrais, vários modelos de DL, como *U-Net* e *DeepMedic*, foram introduzidos. Devido a alguma limitação de desempenho, os modelos de *Convolutional Neural Network* foram desenvolvidos rapidamente nos últimos anos. A determinação automática do tipo de lesão ou área a ela relacionada por meio das imagens é fundamental, pois permite o diagnóstico médico mesmo na ausência de especialistas e no menor tempo possível. É reconhecida a capacidade significativa dos métodos DL nas aplicações de algoritmos baseados em DL na segmentação e classificação de RMI em casos com CCPs e/ou tumores cerebrais. Cabe ressaltar que estratégias como aumento de dados, aprendizado de transferência e adaptação de domínio pode aumentar o desempenho dos métodos de segmentação e classificação baseados em DL e lidar com desafios relacionados a DL, como dados anotados limitados, superajuste e desequilíbrio de classe [71].

O câncer de pele é um dos cânceres mais comuns no mundo, e a incidência está aumentando. A sobrevida em cinco anos pode chegar a 91-95% para o melanoma se for identificado precocemente, o que torna a detecção precoce e o tratamento essenciais para melhorar a sobrevida. O carcinoma escamoso cutâneo apresenta menor risco de disseminação metastática. O carcinoma escamoso cutâneo e o carcinoma basocelular são localmente invasivos, com melhores resultados se tratados em estágio inicial. Várias tecnologias de diagnóstico estão disponíveis para ajudar os clínicos gerais e dermatologistas a identificar com precisão os melanomas, minimizando os atrasos no diagnóstico. O sucesso dessas tecnologias depende de pessoas com lesões cutâneas novas ou em mudança que procuram orientação precoce de profissionais médicos. Aplicativos de smartphones para câncer de pele (“apps”) fornecem uma abordagem tecnológica para ajudar pessoas com lesões suspeitas a decidir se devem procurar mais atendimento médico. Com os smartphones modernos possuindo a capacidade de capturar imagens de alta qualidade, uma variedade de aplicativos de “pele” foi desenvolvida com uma variedade de usos. Esses aplicativos de pele podem fornecer um recurso

de informação, auxiliar no autoexame da pele, monitorar as condições da pele e fornecer conselhos ou orientações sobre a procura de atendimento médico. No entanto, de interesse crescente são os aplicativos de smartphone que usam algoritmos embutidos, ou AI, que catalogam e classificam imagens de lesões em alto ou baixo risco de câncer de pele (geralmente melanoma). O desempenho de aplicativos de smartphone baseados em algoritmos é ruim e variável, o que indica que esses aplicativos ainda não se mostraram promissores o suficiente para recomendar seu uso, sendo que os atuais processos de avaliação da marcação *Conformit Europenne* são inadequados para proteger o público contra os riscos criados pelo uso de aplicativos de diagnóstico de smartphones ou de estratificação de risco [72].

O suporte à decisão clínica é um campo vasto, abrangendo “sistemas de especialistas” e sistemas de alerta e análise de risco, autônomos ou incorporados ao prontuário médico e/ou sistemas de monitoramento de pacientes. Esses sistemas têm grande potencial para auxiliar e aprimorar as habilidades diagnósticas dos médicos, ajudando a superar as limitações de memória humana, distração e fadiga; melhorar a capacidade de fazer cálculos e interpretar dados; e evitar que as decisões sejam afetadas por vieses ou preconceitos. Dentro da radiologia sistemas que fornecem assistência após a análise computadorizada da imagem são geralmente chamados de CAD *systems*. A maioria dos CAD *systems* é desenvolvida para testes de triagem, tarefas repetitivas de correspondência de padrões com uma carga de trabalho de alto volume, potencialmente liberando o tempo dos radiologistas para lidar com tarefas mais complexas. O CAD pode identificar mudanças sutis, mas importantes, que os humanos podem perder e, portanto, tem o potencial de reduzir falsos negativos. O CADx pode oferecer algum benefício aos radiologistas em aplicações de imagem específicas para o diagnóstico de câncer de mama. Não há evidência de efeito benéfico em outras aplicações de CAD e nem evidência de efeito prejudicial. Em última análise, o CAD pode oferecer benefícios apenas em certas situações de diagnóstico, e pode orientar uma análise mais aprofundada para focar na imagem da mama, o que parece ser particularmente bem-sucedido, em detrimento de aplicações como CT pulmonar e imagem dermatológica que não parecem se beneficiar em geral com a adição de CAD, sugerindo que o CAD pode ser melhor aplicado no diagnóstico de câncer usando

imagens [73].

1.3 OBJETIVOS

1.3.1 **Objetivo Geral**

Responder se a assistência mediada por tecnologia traria benefícios no campo da atuação do dentista, especificamente para aqueles que trabalham com pacientes em tratamento de cabeça e pescoço durante a pandemia de COVID-19

1.3.2. **Objetivos Específicos**

1.3.2.1 Avaliar o papel da TO em pacientes com câncer bucal durante a pandemia de COVID-19;
1.3.2.2 Avaliar a viabilidade da telessaúde no monitoramento de pacientes com câncer de cabeça e pescoço sobre a tecnologia remota usada, adesão do usuário, satisfação do usuário e qualidade de vida;
1.3.2.3 Avaliar o uso de ferramentas de inteligência artificial na detecção do câncer comparado aos métodos tradicionais de diagnóstico por imagem;

1.4 METODOLOGIA

A revisão sistemática é um sumário de evidências provenientes de estudos primários conduzidos para responder uma questão específica de pesquisa. Utiliza um processo de revisão de literatura abrangente, imparcial e reprodutível, que localiza, avalia e sintetiza o conjunto de evidências dos estudos científicos para obter uma visão geral e confiável da estimativa do efeito da intervenção [74].

Já a meta-análise é uma análise estatística que combina os resultados de dois ou mais estudos independentes, gerando uma única estimativa de efeito. A meta-análise estima com mais poder e precisão o “verdadeiro” tamanho do efeito da intervenção, muitas vezes não demonstrado em estudos únicos, com metodologia inadequada e tamanho de amostra insuficiente [75].

Ensaio clínico randomizado é um tipo de delineamento de estudo utilizado na realização de RS devido ao fato de ser considerado o padrão de excelência ou padrão ouro para pesquisas em seres humanos [76], entre todos os métodos de investigação clínicas utilizadas, pois é capaz de produzir evidências científicas diretas e com menor probabilidade de erro para esclarecer uma relação causa-efeito entre dois eventos, embora outros delineamentos de pesquisa possam ser utilizados em RS, como, por exemplo, texto e opinião, relato de caso, estudos quase-experimentais e revisões sistemáticas.

As orientações do PRISMA foram seguidas para realização de revisões sistemáticas de diversos delineamentos de estudos, conforme descrito em: http://www.prisma-statement.org/statement.htm., com registro no PROSPERO (www.crd.york.ac.uk/PROSPERO/).

Uma pesquisa ampla foi realizada em bases de dados como PubMed, Cochrane Central Register of Controlled Studies (Cochrane), SciVerse Scopus (Scopus), Web of Science, Latin American and Caribbean Health Sciences (LILACS), Excerpta Medical Database (Embase), Scientific Electronic Library Online (Scielo), Business Source Complete (EBSCOhost) e na literatura cinzenta através do PROQUEST, Google Scholar e JSTOR. Os descritores do Medical Subject Headings (MeSH) foram empregados para desenvolver a estratégia de pesquisa. A busca eletrônica foi padronizada para identificar os artigos relevantes por meio da combinação de todos os descritores. Foi utilizado o software gerenciador de referências online Rayyan QCRI (https://rayyan.qcri.org/welcome) para remoção de duplicatas, além da remoção manual.

A estratégia PICO (População, Intervenção, Comparação e Desfecho) e PIRD (Participante, Teste Índice, Teste de Referência e Diagnóstico de interesse) foi utilizada para definir os critérios de inclusão e exclusão nas revisões realizadas. Foram estabelecidos critérios de inclusão e exclusão de acordo com os objetivos de cada artigo de forma a encontrar os trabalhos mais relevantes sobre os temas

discorridos nos artigos. Os principais desfechos primários considerados foram os benefícios do uso da TO para pacientes em tratamento de câncer de boca e cabeça e pescoço durante a pandemia de COVID-19; modelo de aplicativo já utilizados em TM/Telesaúde; número de pacientes que aderem ao uso; QV e satisfação do paciente no uso do aplicativo de TM/Telesaúde e detecção de câncer e diagnóstico por meio de AI.

A seleção de artigos foi realizada em duas fases. Na fase 1 dois revisores avaliaram títulos e resumos de todos os artigos, de acordo com os critérios de inclusão. Foram removidas referências duplicadas por meio do software online Rayyan QCRI, seguida de uma segunda remoção manual. Dos artigos remanescentes foram lidos os títulos e resumos de acordo com os critérios de elegibilidade, sendo avaliados estudos provenientes da literatura cinzenta. Na fase dois, os dois revisores realizaram leitura na íntegra, excluindo os artigos que não atendiam os critérios de inclusão adotados. Estas etapas foram realizadas de forma independente pelos dois revisores. Na ocorrência de discordância, o artigo foi discutido pelos dois revisores e, na ausência de consenso, analisado por um terceiro revisor de modo que se atingisse uma decisão final. Buscas manuais de listas de referências de artigos relevantes e de teses e dissertações também foram realizadas.

A verificação da qualidade metodológica em estudos individuais foi avaliada pela Lista de Verificação de Avaliação Crítica do Joanna Briggs Institute (Instituto Joanna Briggs, 2014). Os dados foram extraídos dos artigos selecionados e as respostas classificadas pelos parâmetros "yes", "no" ou "unclear", onde “Yes” corresponde a baixo risco de viés, “no” indica alto risco de viés e “unclear” significa risco de viés desconhecido ou não claro. O objetivo desta avaliação é avaliar a qualidade metodológica de um estudo e determinar até que ponto um estudo abordou a possibilidade de viés em seu desenho, condução e análise. Os resultados desta avaliação podem então ser usados, para informar a síntese e interpretação dos resultados do estudo.

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CAPÍTULO 2 - THE ROLE OF TELEDENTISTRY IN ORAL CANCER PATIENTS DURING THE COVID-19 PANDEMIC: AN INTEGRATIVE LITERATURE REVIEW

da Silva HEC, Santos GNM, Leite AF, Mesquita CRM, de Souza Figueiredo PT, Dos Reis PED, Stefani CM, de Melo NS. The role of teledentistry in oral cancer patients during the COVID-19 pandemic: an integrative literature review. Support Care Cancer. 2021 Dec;29(12):7209-7223. doi: 10.1007/s00520-021-06398-0.

2.1 ABSTRACT

Objectives: This Integrative Review aimed to assess the benefits of the use of teledentistry for patients undergoing treatment of oral and head and neck cancer during the COVID-19 pandemic.
Materials and Methods: We searched in PubMed, Cochrane, Scopus, Web of Science, Lilacs, Embase, Open Grey, Google Scholar, and Jstor databases, for studies referring to the management, control, and assistance, through teledentistry, to patients with oral and head and neck cancer during the COVID-19 pandemic.
Results: We found 356 references in the databases, 209 after duplicates removal, 23 met criteria for full-text reading and 11 studies were included for qualitative synthesis, in four categories: virtual visits, use of remote technology, patient´s satisfaction, multidisciplinary approach in teledentistry. We found that 78% of patients currently preferred teledentistry; 92% of patients would recommend the use of video consultation to other patients. The continuity of dental care, the reduction of patient visits to the hospital, the reduction of the risk of infection with the coronavirus, and limitation of face-to-face consultations to protect health professionals are benefits that reinforce the use of teledentistry by health institutions. Two studies showed patients' satisfaction with the use of teledentistry in monitoring cancer patients and showed an improvement in quality of life.
Conclusions: The teledentistry, as a remote technology for monitoring patients with oral and head and neck cancer, is well accepted by patients in preliminary studies. Although these studies pointed out some benefits of using remote technologies for the care of cancer patients, further robust scientific evidence is still needed in this regard.
Keywords: COVID-19, Teledentistry, Telemedicine, Oral Cancer, Head and Neck Cancer, Integrative Review.

2.2 INTRODUCTION

The emergence of the novel coronavirus (SARS-CoV-2) has resulted in a global public health crisis (COVID-19 pandemic), prompting the World Health Organization (WHO) to declare it a public health emergency of international concern. The pandemic has spread exponentially across the world causing, along with the so mentioned health burden, devastating global economic impacts [1]. The SARS-CoV-2 is highly contagious and can spread rapidly via respiratory secretions. Health care workers, particularly dentists, anesthetists, head and neck surgeons, ophthalmologists, and otolaryngologists, are at a high risk of infection [2]. As dental treatments invariably involve close inspection, examination, diagnostic and therapeutic interventions of the naso-oro-pharyngeal region, dental professionals are most susceptible to get infected with coronavirus [3]. Owing to the transmission of COVID-19 through droplets and aerosols, which are inherent features of the dental practice, most of the countries followed a strategy of suspension of all elective dental care services and reserving it only for emergency cases [4].

For patients with cancer who already have decreased immunity, data from China suggest that the new virus poses additional fatal risks. The mortality of patients with cancer was 5.6% compared to 2.3% of the general population [5]. Cancer was actually found to be a major risk factor for COVID-19's severe events in comparison with chronic obstructive pulmonary disease, diabetes, hypertension, and old age, with 39% of patients with cancer experiencing severe events (intensive care unit stays requiring ventilation or death) versus 8% of patients without cancer [6].

In the United States, the Centers for Disease Control and Prevention (CDC) recommended postponing all elective dental procedures [7]. Major American health societies related to clinical oncology, oncology radiology, otolaryngology, head and neck surgery, and oncology surgery have advised that care should be "taken to avoid delays in consultation and treatment which may adversely affect potentially curable patients". Such institutions have encouraged telemedicine (TM) where appropriate; have advised limiting patient care to "time-sensitive and emergent problems" with a recommendation to consider telephone or video-based patient visits [8-15].

Regarding oral cancer, there is a complete absence of literature regarding the long-term impact of pandemics on patients with oral potentially malignant disorders (OPMDs) and early-stage oral cancer. Prior to this pandemic, even with readily available access for most patients to a fully intact health care infrastructure, less than 50% of patients with oral cancer were diagnosed at an early stage [16].

In this context, TM gains importance, as a valuable tool in the initial assessment of the patient and in the diagnosis of oral medicine conditions [17]. The popularity and prevalence of TM have grown rapidly during this pandemic as many physicians have sought ways to maintain a continuum of care with their patients [18]. Such initiatives have previously been shown to decrease costs, decrease visit time, and lead to high patient satisfaction in surgical fields [10, 20].

This study aimed to analyze, through an integrative literature review, the management, control, and assistance performed by the dental team, through teledentistry (TD), to patients with oral and head and neck cancer during the COVID-19 pandemic. The intention of this study was to answer the following question: “What are the benefits of the use of teledentistry for patients undergoing treatment of oral and head and neck cancer during the COVID-19 pandemic?”

2.3 METHODS

We conducted an integrative review (IR), a distinct unique method in which it is possible to summarize various studies to provide a more extensive understanding of a particular health problem [21]. To perform this IR, we have followed six steps: formulating the research question, searching the literature, extracting data from the primary studies, assessing the studies included in the IR, analyzing, and synthesizing the results, and presenting the IR [22]. The protocol of this study was registered on the Center for Open Science website (https://www.cos.io/), under the DOI number 10.17605/OSF.IO/BP5AN. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [23] was adapted and used to report this IR since there is not a specific checklist to this literature review method yet.

Terminology Definition

TM can be defined as the set of telematic technologies used to provide the patient with health care services – diagnosis, monitoring, therapy – at distance. It is therefore a distance delivery of health services. For the World Health Organization, TM literally means “remote healing” and indicates the use of technologies, information, and communication to improve the health outcomes of patients, increasing access to medical care and information [24]. TD (a subunit of telehealth along with TM) is the remote facilitating of dental care, guidance, education, or treatment via the use of information technology rather than through direct face-to-face contact with any patient [25]. Over the years, TD has proved to be beneficial for remote dental screening, making diagnosis, providing consultation, and proposing treatment plan [26, 27]. For this review, the concept of TD was standardized, acting on both dental and non-dental complications located in the oral cavity as a standard for conducting the search, selection, and analysis of studies.

Research Question

The research question used to perform this IR was: “What are the benefits of the use of teledentistry for patients undergoing treatment of oral and head and neck cancer during the COVID-19 pandemic?”

Search Strategy

On October 19th, 2020, it was performed a broad search of studies without language restrictions in the following databases: PubMed, Cochrane, Scopus, Web

of Science, Lilacs (Latin American and Caribbean Literature), Embase, Library, and grey literature through Open Grey, Google Scholar, and Jstor. The search strategy used is in Additional file 1. It was also done a manual track down of lists of relevant articles. Immediately after the literature investigation, the references were exported to the online reference manager Rayyan QCRI (https://rayyan.qcri.org/welcome) and duplicated references were removed.

Inclusion And Exclusion Criteria

We considered eligible for this IR, studies referring to the performance, management, control, and assistance through TD delivered by dental surgeons (specialized in oral and maxillofacial surgery or members of a multidisciplinary oncology treatment team) to patients with oral and head and neck cancer during the COVID-19 pandemic. The stipulated period for applying the search strategies in the databases was from October 2019 to September 2020, due to the beginning of COVID-19 infection and subsequent pandemic.

Exclusion criteria comprised: (1) In vitro studies; (2) Studies in animal models; (3) Guidelines, abstracts, book chapters, research protocols, and posters; (4) Studies evaluating other medical/dental specialties; (5) Studies with telemonitoring of other types of primaries cancer; (6) Telemonitoring's studies of other comorbidities (heart failure, Chronic Obstructive Pulmonary Disease (COPD), HIV, obstetric disease, asthma, hypertension, diabetes, *etc*.); (7) Studies evaluating the use of TD for telediagnosis; (8) Monitoring of oral and head and neck cancers performed by other professionals (otolaryngologists, nurses, *etc.*); (9) Studies evaluating oral cancer or head and neck cancer with subjects unrelated to TD.

Study Selection

The articles' selection was performed in two phases. In phase 1, two independent reviewers (HECS and GNMS) screened titles and abstracts of all studies, according to the eligibility criteria. In phase 2, both reviewers (HECS and GNMS) independently read the full texts according to the inclusion and exclusion criteria. In case of disagreements, both reviewers discussed and, if consensus was not reached, a third reviewer (AFL) analyzed the studies to reach a final decision.

Data Collection Process And Items

It was also performed data extraction by two independent reviewers (HECS and GNMS) and posteriorly compared. Extracted data comprised author, year, country; features of users and professionals who use remote technology; security criteria required by remote technology; groups (n*) and treatments; remote technology used or deployed; description of the use of the remote technology adopted and main conclusions of each paper.

Eligibility

The electronic search of five databases resulted in 356 references. Removal of duplicated studies resulted in 209 references. Titles and abstracts from these studies were read and those not fulfilling the eligibility criteria were excluded. In addition, grey literature was searched. Jstor and Open Grey returned no references. From Google Scholar, the first 100 references were considered for evaluation. At the end of phase 1, 23 studies remained for full-text reading (phase 2). A manual search of reference lists did not provide additional studies. Full-text reading resulted in 11 eligible studies for qualitative analysis. Additional file 2 presents a list of excluded

articles and reasons for exclusion. A flowchart of the complete process is shown in Figure 1.

Assessing The Methodological Quality Of Included Studies

To assess the methodological quality of the studies, the Joanna Briggs Institute (JBI) - Critical Appraisal Tools (Joanna Briggs Institute, 2014) tools were used [28, 29]. Two review authors (HECS and GNMS) independently assessed the methodological quality of the included studies, using the checklists corresponding to the designs of the included studies, namely: JBI critical appraisal checklist for case reports [28], JBI critical appraisal checklist for Text and Opinion [29]. Disagreements were resolved by discussion and, where necessary, a third review author (AFL) was consulted. Data were extracted from selected articles and the answers were classified using the parameters “yes”, “no” or “unclear”. “Yes” corresponded to high quality, “no” low quality, and “unclear” unknown or unclear quality.

The purpose of this appraisal is to assess the methodological quality of a study and to determine the extent to which it has addressed the possibility of bias in its design, conduct, and analysis. The results of this appraisal can then be used to inform synthesis and interpretation of the results of the study [28]. Scoring decisions were agreed upon by all reviewers before the critical appraisal commenced, and studies were characterized according to the following: (a) high methodological quality, if studies reached more than 70% scores of “yes”; (b) moderate methodological quality, if “yes” scores were between 50% and 69%; and (c) low methodological quality, if “yes” scores were below 49% [30].

2.4 RESULTS

Study Characteristics

Included studies were conducted in Brazil [31, 36, 39], England [32], Hong Kong [34], Italy [33, 37], India [35], Saudi Arabia [4], and United States [38, 40], all published in English.

Seven references were letters to the editor/editorials [4, 31, 32, 35-37, 39], and four were case reports [33, 34, 38, 40] evaluating the application of remote technologies in the follow-up and monitoring of patients with oral cancer and head and neck cancer during the COVID-19 pandemic. The emphasis was on the mitigation of the evolution, severity, and complexity of the disease in the face of restrictions that the pandemic imposed on health systems. Table 1 summarizes details of studies regarding author, year, country; features of users (patients) and professionals who used remote technology; security criteria required by remote technology; groups (n*) and treatments; remote technology used or deployed; description of the use of the remote technology adopted; main conclusions.

Overview Of The Findings

Oral cancer patients have a complex demand for care. Many of these demands include the dental procedures prior to cancer treatment, management, and prevention of side effects linked to cancer treatment, such as mucositis, infections, complications related to jaw osteonecrosis, uncontrolled pain, and follow-up of the patient after the treatment in control over time. The social distancing and the need generated by the COVID-19 pandemic to remain at home generated a difficulty in conducting face-to-face consultations, which leads to the possibility of delay in the treatment of patients with oral cancer. TD emerges as an alternative to this demand, which is urgent given the current situation of social isolation [4, 36, 35].

The studies were divided into four categories, accordingly with the theme related to TD, as follows: 1) Virtual visits, 2) Use of remote technology, 3) Patient's Satisfaction, and 4) Multidisciplinary approach in teledentistry.

Virtual Visits

Some authors have observed that dentists may carry out virtual visits for follow-up, interviews, clinical examinations with the guidance of oral habits for their patients [4, 35]. Two authors verified that patients could take photographs and copy of biopsy report [33, 40] of the mouth and refer them to the dentist to manage the evolution of the lesion. According to the authors, this also allows the control of the virtual education of the patients about the clinical signs and risk factors of oral cancer, through valid and reliable websites, reducing anxiety with information available in the common media [4, 35] and a spatial appreciation of in some oral lesions through using the mobile phone light, allowing the humanization of the virtual visit [40].

The authors found that virtual visits are an alternative to providing oral medicine care with the effective screening of potentially urgent cases. Teleassistance promotes better patient-professional communication before, during and after cancer care [36] to maintain and improve patient's quality of life [35]. The authors believe that the assistance of the virtual visit to cancer patients, could help to prioritize the ones with highly suspected malignant lesions, avoiding face-to-face contact, with referral for clinical examination and appropriate procedures [36, 39].

In another strategy evaluated in a study conducted at a hospital in Hong Kong, the authors realized that virtual visits could monitor the use of medications, thus reducing patient's hospital attendance to minimize the risk of cross infection [34]. Thus, the authors recommended, according to the complexity of each case, that follow-up consultations of cancer patients undergoing treatment with oral antineoplastic drugs should be carried out telematically [37]. TM can provide preoperative counseling, education on postoperative care, dietary advice and exercise recommendations for neck and shoulders. In the postoperative phase:

simple wound review and troubleshooting [34].

Use Of Remote Technology

Several remote technologies were used by included studies to conduct TD consultations. In a research [32], the author perceived that the telephone is one of the easiest alternatives and can be associated with a structured guide, as the PCI-HN (a list of items rather than questions that facilitates communication over the phone). The aim is to help standardize and guide consultation, assist multiprofessional communication and prevent the loss of relevant information. The advantage is the reduction of face-to-face consultations in order to limit the spread of COVID-19 and protect patients and clinical staff, reduce travel costs for patients to the hospital and support providers to focus on a particular location, carry out the consultations by less experienced staff members and the PCI-HN allows doctors to continue working at home.

In a study [34] conducted in Hong Kong, the authors used video conference applications like Zoom app for virtual consultations to avoid constant rescheduling of face-to-face consultations. The authors recommended to use the latest version of the *Zoom client* with a corporate account to enjoy enterprise security features, setting a password for every meeting and the “Lock” function enabled to avoid meeting intrusion.

In a study [31] conducted in the state of Santa Catarina, Brazil, the authors used TD models to increase the coverage of oral oncology services. The Santa Catarina State Integrated Telemedicine and Telehealth System (STT / SC) serves 100% of the municipalities, and it integrates primary, secondary, and tertiary healthcare facilities in a single infrastructure. This module has the functions of collecting clinical data by the dentist at the primary health units; provide remote support by a specialist to manage the clinical conditions that can be treated in primary healthcare units and promote appropriate referral of patients to secondary health units, complying with the security criteria, according to the Brazilian regulations.

Patient's Satisfaction

In a study [33] conducted at the University of Catanzaro, Italy, regarding patient satisfaction with the use of TD, the authors observed that, in a sample of 90 patients, 73% considered as easy to participate in the consultation, 20% moderate and 7% difficult. TD was the patients' preferred type of consultation (78%), followed by indigenous (12%) and face-to-face appointment (12%). 80% of patients preferred videophone over the telephone examinations, and 92% would recommend video calling to others. Patients were often very grateful for TD visits, and no TD consultation has requested a visit in person for status verification or follow-up [38].

Multidisciplinary Approach In TD

Three studies [34, 35, 38] indicated that communication with colleagues in a multidisciplinary way is essential to anticipate barriers, prepare contingency plans, evaluate their effectiveness, and refine/review operations as needed. Multidisciplinary tumor councils, academic meetings, or multidisciplinary tumor board meetings can meet regularly via applications, such as Zoom, which guarantees communication, compensation, and consensus for optimal patient care during the pandemic. However, one author [34] highlighted another way of multidisciplinary approach, the collaboration in the distribution of priority patients with head and neck cancer between different regional units to provide timely surgery, optimizing treatment during the pandemic.

Table 2 shows the summary of the benefits of using TD to monitor patients with oral and head and neck cancer.

Methodological Quality Assessment Among Studies

None of the studies fulfilled all methodological quality criteria. However, the overall average of “yes” answers of the studies was 80%, and most assessed high quality. Only one study [38] was considered to be of moderate quality and one [40] to be of low methodological quality.

None of the studies [4, 31, 32, 35-37, 39] assessed by the text and opinion checklist showed any inconsistency with the logically defended literature/sources.

Regarding the evaluation of the Methodological quality tool for Case Reports, two studies [38, 40] did not present patients’ demographic characteristics clearly described. Three studies [33, 37, 39] did not show patients’ history clearly described and presented as a timeline. Two studies [33, 40] were unclear for the post-intervention clinical condition and for diagnostic tests or assessment methods, respectively, and two studies [38, 40] did not clearly report the demographics of the participants. More information on methodological quality can be found in Table 3 (summarized assessment).

2.5 DISCUSSION

This IR evaluated the management, control, and assistance, through TD, of patients with oral and head and neck cancer during the COVID-19 pandemic. The aim was to assess the benefits of the use of TD for patients undergoing treatment of oral and head and neck cancer during the COVID-19 pandemic. Included studies showed that TD applied to the monitoring of patients with oral cancer and head and neck cancer was a useful tool in supporting patients during this pandemic period, with improved general well-being and quality of life.

As a remote technology for monitoring patients with oral and head and neck cancer, TD was well accepted by patients and professionals in preliminary studies. The benefits presented in this review are the continuity of dental care, reduced travels to the hospital for patient care, reduced risk of infection with the coronavirus, and limitation of face-to-face consultations to protect health professionals, among

others.

Three studies discussed concerns on the safety of data exchanging between professionals and patients during the use of TD, either with a TeleHealth system [31], by Zoom video conference [34], or messaging applications like WhatsApp [33]. Photos and image encryption restrictions of people's access to smartphones, and count corporate applications were used to increase the exchange data security [31, 33] while following the legislation regarding the guarantee of data privacy [31, 34].

TD has advantages not only during the COVID-19 pandemic because it reaches other aspects of dental care, benefiting patients in different situations. When providing low-cost, large-scale specialist support to primary public healthcare units, TD guarantees access to technology by low-income people, which optimizes care, reduces the waiting time for an appointment and increases the resolution of the clinical case [31].

Activities such as further preoperative counseling, education of postoperative care, dietary advice, and neck and shoulder exercise recommendations could all be delivered by TD. In the postoperative phase, simple wound review and troubleshooting could also be performed [34]. The TM is well accepted especially by the patients residing in areas rather far from the health units, who had to travel a long way and, above all, be exposed to other patients who could be carriers of COVID-19 and other infectious agents [33]. It can be pointed out as advantages of TD the reduced face-to-face consultations to limit the spread of COVID-19 and protect the patients and the clinical teams. The consultations may be completed by less experienced members of the team including use in the nurse-led clinics. Consequently, experienced staff would become free to aid clinical and workforce planning in other pressure points [32].

The introduction of the telemedicine service is considered very beneficial, especially in terms of patient triage. The interruption of dental activities by health authorities leads to a decrease in the care of oncological patients who need treatment, focusing only on emergencies. There is a significant reduction in dental care, periodontal maintenance, and patient care at the oral disease clinic. However, this decrease is gradually offset by the growing telemedicine service. In this context, there is an increase in patient abstention from attending consultations to avoid the risk of infection. This fact is accentuated by restrictive measures by health authorities

to protect patients at risk and staff. After an average period of 4 weeks of minimal activity, an increase in the flow of patients is observed, probably due to the increased demand for emergency dental treatment, despite the increasing number of active COVID-19 patients and related deaths during the pandemic [41].

However, TD in monitoring patients with oral cancer and head and neck cancer presents challenges that need to be overcome. The lack of acceptance of TD by the dentists can be attributed to the fact that they may find it complex and may be resistant to new skills acquisition demand [42, 43]. They may be technologically challenged, afraid of making an inaccurate case evaluation, and concerned about increased costs and expenses. There may be constraints related to infrastructure, as poor internet access, shortage of hardware, lack of training, lack of technical support and expertise. Organizational incompatibility of TD with the healthcare system, insufficient financial reimbursement, inadequate guidelines in coordination between remote and core center, and high cost of setup are other challenges related to its acceptance by dentists [43].

Two-dimensional representation of lesions and inability to perform tests like palpation, percussion and auscultation are other limitations [26]. Even with imaging technology, it may be challenging to visualize certain mucosal areas [44]. Some professionals reported that they were not satisfied making a diagnosis using telecommunication images without clinical information. Access to patient information is one of the main limitations that could affect the validity of TD. Face-to-face examinations provide an opportunity to talk with patients to obtain information essential to diagnosis. Lack of information could decrease the dental professional's confidence in making a diagnosis using only a TD system and therefore diminishes the validity score of TD [27].

There is a difference between the benefits of using TD and the face-to-face clinical examination. Oral lesions, especially those with the potential for malignancy, are not effectively monitored by TD alone. In these situations, TD has the potential to ensure only a temporary adjustment until the clinical examination is possible to be performed in person.

In the case of the lack of acceptance of TD by patients, the difficulty of face-to-face communication may lead patient apprehension regarding the inadequacy of proper communication of their problems to their dentists. Elderly Patients, for

example, may experience technology anxiety, isolation, feelings of neglect and fears, difficulties regarding the delay in cancer treatment and access to support services during this pandemic period. Acceptability of TD by the patients will increase in parallel with the acceptability of telemedicine in general, which is increasing day-by-day [32, 45].

Two studies inferred the role of TD in the context of multi-professional and multi-institutional collaboration in monitoring patients with oral cancer and head and neck cancer. TD plays a decisive role in reducing the risk of spreading COVID-19. In this period of health emergency, the treatment of head and neck cancer [33] has shown a multidisciplinary approach (maxillofacial surgeon, radiotherapist, oncologist, nutritionist, *etc.*), through the involvement of other specialists in the videoconference and/or photography. It should be noted that novel methods, such as TD and regional collaboration with other centers have been implemented with some success, in order to achieve the targeted waiting times to arrange early surgery for more urgent cases in different hospitals with a relief of the number of pending head and neck cancer operations by 20% [34, 37, 38].

Two studies presented patient's satisfaction with the use of remote technology in the debate between TD and the monitoring of cancer patients. It should be highlighted that constant check-ups, counseling, and support can be performed through TD consultations to maintain and improve the general well-being of patients and, consequently, quality of life [35]. The high percentage of satisfaction that emerged from the analysis of the satisfaction questionnaires administered to the patient shows that TD was well accepted. Above contact, although remotely, has positively influenced the patient's state of well-being, motivation, and sense of security, especially in this uncertain period [33].

These preliminary data corroborate current literature, suggesting a high satisfaction from both healthcare staff and service users [44, 46]. It can aid not only patient education but also contribute to diagnosis and treatment [39] in association with a possible face-to-face consultation for a definitive diagnosis, when necessary. There are limitations to real-time interactive video consultations in diagnosing disease and assessing patient problems, particularly in a dental context. The TD model has some limitations, such as the inability to approach texture and clearly delineate the borders of a lesion, particularly in the posterior oral cavity, with an

unreliable data connection and poor image quality. Factors linked to the patient, such as the ability to connect to the software, lighting, manual dexterity, familiarity with mobile/tablet devices, and the knowledge of the service user to attend technology-based consultations. Due to these considerations, video conferencing has a limited role and should be used with care [33, 47].

The accessibility of oral cavity to user-friendly imaging devices makes telemedicine an appealing solution for the management of secondary lesions as oral mucositis. Given the popularity of mobile phone-integrated cameras, the idea of obtaining images of the oral surfaces seems feasible, however, the quality of these photos does not enable us to apply this concept universally [48].

As a limitation in carrying out the IR, it is possible to point out the few existing studies in the literature correlating TD and the monitoring of patients with oral cancer and head and neck cancer, both in the direct care of dental complications during cancer treatment and by aggravation caused by the cancer treatment itself. It is suggested that professionals involved and monitoring the quality of life of patients throughout cancer treatment carry out studies with a greater emphasis on the use of remote technology aimed at dentistry with the assessment of patient satisfaction, as a way of verifying the effectiveness of the use of TD.

2.6 CONCLUSION

TD, as a remote technology for monitoring patients with oral and head and neck cancer, is well accepted by patients and professionals in preliminary studies. The benefits presented in this IR are the continuity of dental health monitoring, reduced travel for patient care in the hospital, reduced risk of infection with the coronavirus, and limitation of face-to-face consultations to protect health professionals, among others. Nevertheless, this alternative of care presents many challenges, such as the lack of acceptance of TD by the dentists, fear of making an inaccurate diagnosis, concerns about increased costs, expenses, and necessary infrastructure, insufficient financial reimbursement, inadequate guidelines. For the patients, the technology anxiety, isolation, feelings of neglection and fears, difficulties regarding the delay in cancer treatment, and access to support services during the

COVID-19 pandemic should be considered. It is emphasized that studies with more robust scientific evidence are necessary to consolidate the benefits of using remote technologies for monitoring as a viable alternative for the monitoring of cancer patients.

Declarations

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Consent to participate: Not applicable.
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Code availability: Not applicable.

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Appendix 1- Database search strategy.

Database	Search (October the 19th, 2020)	References
PubMed	Filters: in the last 1 year - ("Oral Oncology"[All Fields] OR "Head and Neck Oncology"[All Fields] OR "Mouth Neoplasms"[All Fields] OR "Mouth Neoplasm"[All Fields] OR "neoplasm mouth"[All Fields] OR "neoplasms oral"[All Fields] OR "neoplasm oral"[All Fields] OR "Oral Neoplasm"[All Fields] OR "Oral Neoplasms"[All Fields] OR "neoplasms mouth"[All Fields] OR "Cancer of Mouth"[All Fields] OR "Mouth Cancers"[All Fields] OR "Oral Cancer"[All Fields] OR "cancer oral"[All Fields] OR "cancers oral"[All Fields] OR "Oral Cancers"[All Fields] OR "Cancer of the Mouth"[All Fields] OR "Mouth Cancer"[All Fields] OR "cancer mouth"[All Fields] OR "cancers mouth"[All Fields] OR "Head and Neck Neoplasms"[All Fields] OR "neoplasms head and neck"[All Fields] OR "head neck neoplasms"[All Fields] OR "Cancer of Head and Neck"[All Fields] OR "Head and Neck Cancer"[All Fields] OR "Cancer of the Head and Neck"[All Fields] OR "Upper Aerodigestive Tract Neoplasms"[All Fields] OR "UADT Neoplasms"[All Fields] OR "neoplasms uadt"[All Fields] OR "Head Neoplasms"[All Fields] OR "neoplasms head"[All Fields] OR "Neck Neoplasms"[All Fields] OR "neoplasms neck"[All Fields] OR "Cancer of Head"[All Fields] OR "Head Cancer"[All Fields] OR "Cancer of the Head"[All Fields] OR "Cancer of Neck"[All Fields] OR "Neck Cancer"[All Fields] OR "Cancer of the Neck"[All Fields] OR "Malignant Disorders"[All Fields] OR "Precancerous Conditions"[All Fields] OR ("Precancerous Conditions"[MeSH Terms] OR ("precancerous"[All Fields] AND "conditions"[All Fields]) OR "Precancerous Conditions"[All Fields] OR "premalignant"[All Fields] OR "premalign"[All Fields] OR "premalignancies"[All Fields] OR "premalignancy"[All Fields]) OR ("Precancerous Conditions"[MeSH Terms] OR ("precancerous"[All Fields] AND "conditions"[All Fields]) OR "Precancerous Conditions"[All Fields] OR "premalignant"[All Fields] OR "premalign"[All Fields] OR "premalignancies"[All Fields] OR "premalignancy"[All Fields]) OR ("Precancerous Conditions"[MeSH Terms] OR ("precancerous"[All Fields] AND "conditions"[All Fields]) OR "Precancerous Conditions"[All Fields] OR "premalignant"[All Fields] OR "premalign"[All Fields] OR "premalignancies"[All Fields] OR "premalignancy"[All Fields]) OR ("Precancerous Conditions"[MeSH Terms] OR ("precancerous"[All Fields] AND "conditions"[All Fields]) OR "Precancerous Conditions"[All Fields] OR "premalignant"[All Fields] OR "premalign"[All Fields] OR "premalignancies"[All Fields] OR "premalignancy"[All Fields])) AND ("Teledentistry"[All Fields] OR "Tele-dentistry"[All Fields] OR "Tele-triage"[All Fields] OR "Teletriage"[All Fields] OR ("triage"[MeSH Terms] OR "triage"[All Fields] OR "triages"[All Fields] OR "triaged"[All Fields] OR "triaging"[All Fields]) OR ("telemedicine"[MeSH Terms] OR "telemedicine"[All Fields] OR "telemedicine s"[All Fields]) OR "Tele-medicine"[All Fields] OR "Mobile Health"[All Fields] OR "health mobile"[All Fields] OR "Mhealth"[All Fields] OR ("telehealth s"[All Fields] OR "telemedicine"[MeSH Terms] OR "telemedicine"[All Fields] OR "telehealth"[All Fields]) OR "Tele-health"[All Fields] OR ("telemedicine"[MeSH Terms] OR "telemedicine"[All Fields] OR "ehealth"[All Fields]) OR ("telemonitor"[All Fields] OR "telemonitored"[All Fields] OR "telemonitoring"[All Fields] OR "telemonitors"[All Fields]) OR ("telementor"[All Fields] OR "telementored"[All Fields] OR "telementoring"[All Fields]) OR "Teleassistance"[All Fields] OR "Tele-assistance"[All Fields])	71
Cochrane Library	("Oral Oncology" OR "Head and Neck Oncology" OR "Mouth Neoplasms" OR "Mouth Neoplasm" OR "Neoplasm, Mouth" OR "Neoplasms, Oral" OR "Neoplasm, Oral" OR "Oral Neoplasm" OR "Oral Neoplasms" OR "Neoplasms, Mouth" OR "Cancer of Mouth" OR "Mouth Cancers" OR "Oral Cancer" OR "Cancer, Oral" OR "Cancers, Oral" OR "Oral Cancers" OR "Cancer of the Mouth" OR "Mouth Cancer" OR "Cancer, Mouth" OR "Cancers, Mouth" OR "Head and Neck Neoplasms" OR "Neoplasms, Head and Neck" OR "Head, Neck Neoplasms" OR "Cancer of Head and Neck" OR "Head and Neck Cancer" OR "Cancer of the Head and Neck" OR "Upper Aerodigestive Tract Neoplasms" OR "UADT Neoplasms" OR "Neoplasms, UADT" OR "Head Neoplasms" OR "Neoplasms, Head" OR "Neck Neoplasms" OR "Neoplasms, Neck" OR "Cancer of Head" OR "Head Cancer" OR "Cancer of the Head" OR "Cancer of Neck" OR "Neck Cancer" OR "Cancer of the Neck" OR "Malignant Disorders" OR "Precancerous Conditions" OR Premalignant OR Premalign OR Premalignancies OR Premalignancy) in Title Abstract Keyword AND (Teledentistry OR Tele-dentistry OR Tele-triage OR Teletriage OR Triaging OR Telemedicine OR Tele-medicine OR "Mobile Health" OR "Health, Mobile" OR "Mhealth" OR Telehealth OR Tele-health OR Ehealth OR Telemonitoring OR Telementoring OR Teleassistance OR Tele-assistance) in Title Abstract Keyword - with Cochrane Library publication date Between Oct 2019 and Oct 2020 (Word variations have been searched)	7 *(continued)*

Appendix 1- Database search strategy.

Database	Search (October the 19th, 2020)	References
Scopus	(TITLE-ABS-KEY(("Oral Oncology" OR "Head and Neck Oncology" OR "Mouth Neoplasms"OR"Mouth Neoplasm" OR "Neoplasm, Mouth" OR "Neoplasms, Oral" OR "Neoplasm, Oral" OR "Oral Neoplasm" OR "Oral Neoplasms" OR "Neoplasms, Mouth" OR "Cancer of Mouth" OR "Mouth Cancers")) OR TITLE-ABS-KEY (("Oral Cancer" OR "Cancer, Oral" OR "Cancers, Oral" OR "Oral Cancers" OR "Cancer of the Mouth" OR "Mouth Cancer" OR "Cancer, Mouth" OR "Cancers, Mouth" OR "Head and Neck Neoplasms" OR "Neoplasms, Head and Neck" OR "Head, Neck Neoplasms")) OR TITLE-ABS-KEY (("Cancer of Head and Neck"OR"Head and Neck Cancer" OR "Cancer of the Head and Neck" OR "Upper Aerodigestive Tract Neoplasms" OR "UADT Neoplasms" OR "Neoplasms, UADT" OR "Head Neoplasms" OR "Neoplasms, Head" OR "Neck Neoplasms" OR "Neoplasms, Neck")) OR TITLE-ABS-KEY (("Cancer of Head" OR "Head Cancer" OR "Cancer of the Head" OR "Cancer of Neck" OR "Neck Cancer" OR "Cancer of the Neck" OR "Malignant Disorders" OR "Precancerous Conditions" OR premalignant OR premalign OR premalignancies OR premalignancy)) AND TITLE-ABS-KEY((teledentistry OR tele-dentistry OR tele-triage OR teletriage OR triaging OR telemedicine OR tele-medicine OR "Mobile Health" OR "Health, Mobile" OR "Mhealth" OR telehealth OR tele-health OR ehealth OR telemonitoring OR telementoring OR teleassistance))) AND (LIMIT-TO (PUBYEAR,2020) OR LIMIT-TO (PUBYEAR, 2019))	84
Web of Science	#1-TS=("Oral Oncology" OR "Head and Neck Oncology" OR "Mouth Neoplasms" OR "Mouth Neoplasm" OR "Neoplasm, Mouth" OR "Neoplasms, Oral" OR "Neoplasm, Oral" OR "Oral Neoplasm" OR "Oral Neoplasms" OR "Neoplasms, Mouth" OR "Cancer of Mouth" OR "Mouth Cancers" OR "Oral Cancer" OR "Cancer, Oral" OR "Cancers, Oral" OR "Oral Cancers" OR "Cancer of the Mouth" OR "Mouth Cancer" OR "Cancer, Mouth" OR "Cancers, Mouth" OR "Head and Neck Neoplasms" OR "Neoplasms, Head and Neck" OR "Head, Neck Neoplasms" OR "Cancer of Head and Neck" OR "Head and Neck Cancer" OR "Cancer of the Head and Neck" OR "Upper Aerodigestive Tract Neoplasms" OR "UADT Neoplasms" OR "Neoplasms, UADT" OR "Head Neoplasms" OR "Neoplasms, Head" OR "Neck Neoplasms" OR "Neoplasms, Neck" OR "Cancer of Head" OR "Head Cancer" OR "Cancer of the Head" OR "Cancer of Neck" OR "Neck Cancer" OR "Cancer of the Neck" OR "Malignant Disorders" OR "Precancerous Conditions" OR Premalignant OR Premalign OR Premalignancies OR Premalignancy) *Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=2019-2020* #2- TS=(Teledentistry OR Tele-dentistry OR Tele-triage OR Teletriage OR Triaging OR Telemedicine OR Tele-medicine OR "Mobile Health" OR "Health, Mobile" OR "Mhealth" OR Telehealth OR Tele-health OR Ehealth OR Telemonitoring OR Telementoring OR Teleassistance OR Tele-assistance) *Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=2019-2020* #3- #2 AND #1 *Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=2019-2020*	48
Lilacs (Spanish)	(“Cáncer bucal” OR “Cáncer de cavidad bucal” OR “Neoplasia bucal” OR “Neoplasia de cavidad bucal” OR “Neoplasia Cavidad oral” OR “Neoplasia de la boca” OR “Neoplasia de la cavidad oral” OR “Neoplasias de la boca” OR “Neoplasias de la cavidad oral” OR "Tumor oral" OR "Tumor de la cavidad oral" OR "Tumor de la boca" OR "Tumores orales" OR "Tumores de la boca" OR "Cáncer de cabeza" OR "Cáncer de cabeza y cuello" OR "Cáncer de cuello" OR "Neoplasias del cuello" OR "Neoplasias del tracto aerodigestivo superior") [Palavras] and (Teleodontología OR Telemedicina OR "Salud Móvil" OR "Salud Mueble" OR "mSalud"OR Telesalud OR "eSalud" OR Telemonitorización OR Teleasistencia) [Palavras]	0
Lilacs (Portuguese)	(“Câncer Bucal” OR “Câncer Oral” OR “Câncer da Cavidade Bucal” OR “Câncer da Cavidade Oral” OR “Câncer de Cavidade Oral” OR “Neoplasia Bucal” OR “Neoplasia Oral” OR “Neoplasia da Cavidade Bucal” OR “Neoplasia da Cavidade Oral” OR “Neoplasia de Boca” OR “Neoplasia de Cavidade Bucal” OR “Neoplasia de Cavidade Oral” OR “Neoplasias Orais” OR “Neoplasias da Boca” OR “Neoplasias da Cavidade Bucal” OR “Neoplasias da Cavidade Oral” OR Neoplasias de Boca” OR “Tumor Bucal” OR “Tumor Oral” OR “Tumor da Cavidade Bucal” OR “Tumor da Cavidade Oral” OR “Tumor de Boca” OR “Tumores Bucais” OR “Tumores Orais” OR “Tumores da Boca” OR “Tumores da Cavidade Bucal” OR “Tumores da Cavidade Oral” OR “Câncer da Cabeça“ OR “Câncer de Cabeça e Pescoço“ OR “Câncer do Pescoço“ OR “Neoplasias do Pescoço“ OR “Neoplasias do Trato Aerodigestório Superior“) [Palavras] and (Teleodontologia OR Tele-Odontologia OR Teletriagem OR Tele-triagem OR	0

(continued)

Appendix 1- Database search strategy.

Database	Search (October the 19th, 2020)	References
	Telemedicina OR "Saúde Móvel" OR "mSaúde" OR Telessaúde OR Tele-saúde OR eSaúde OR Tele-Monitoramento OR Telementoria OR Teleassistência OR Tele-assistência) [Palavras]	
EMBASE	#1- (((((('oral oncology':ti,ab,kw OR head:ti,ab,kw) AND 'neck oncology':ti,ab,kw OR 'mouth neoplasms':ti,ab,kw OR 'mouth neoplasm':ti,ab,kw OR 'neoplasm, mouth':ti,ab,kw OR 'neoplasms, oral':ti,ab,kw OR 'neoplasm, oral':ti,ab,kw OR 'oral neoplasm':ti,ab,kw OR 'oral neoplasms':ti,ab,kw OR 'neoplasms, mouth':ti,ab,kw OR 'cancer of mouth':ti,ab,kw OR 'mouth cancers':ti,ab,kw OR 'oral cancer':ti,ab,kw OR 'cancer, oral':ti,ab,kw OR 'cancers, oral':ti,ab,kw OR 'oral cancers':ti,ab,kw OR 'cancer of the mouth':ti,ab,kw OR 'mouth cancer':ti,ab,kw OR 'cancer, mouth':ti,ab,kw OR 'cancers, mouth':ti,ab,kw OR head:ti,ab,kw) AND 'neck neoplasms':ti,ab,kw OR 'neoplasms, head':ti,ab,kw) AND neck:ti,ab,kw OR 'head, neck neoplasms':ti,ab,kw OR 'cancer of head':ti,ab,kw) AND neck:ti,ab,kw OR head:ti,ab,kw) AND 'neck cancer':ti,ab,kw OR 'cancer of the head':ti,ab,kw) AND neck:ti,ab,kw OR 'upper aerodigestive tract neoplasms':ti,ab,kw OR 'uadt neoplasms':ti,ab,kw OR 'neoplasms, uadt':ti,ab,kw OR 'head neoplasms':ti,ab,kw OR 'neoplasms, head':ti,ab,kw OR 'neck neoplasms':ti,ab,kw OR 'neoplasms, neck':ti,ab,kw OR 'cancer of head':ti,ab,kw OR 'head cancer':ti,ab,kw OR 'cancer of the head':ti,ab,kw OR 'cancer of neck':ti,ab,kw OR 'neck cancer':ti,ab,kw OR 'cancer of the neck':ti,ab,kw OR 'malignant disorders':ti,ab,kw OR 'precancerous conditions':ti,ab,kw OR premalignant:ti,ab,kw OR premalign:ti,ab,kw OR premalignancies:ti,ab,kw OR premalignancy:ti,ab,kw) AND [2019-2020]/py #2-(teledentistry:ti,ab,kw OR 'tele dentistry':ti,ab,kw OR 'tele triage':ti,ab,kw OR teletriage:ti,ab,kw OR triaging:ti,ab,kw OR telemedicine:ti,ab,kw OR 'tele medicine':ti,ab,kw OR 'mobile health':ti,ab,kw OR 'health, mobile':ti,ab,kw OR 'mhealth':ti,ab,kw OR telehealth:ti,ab,kw OR 'tele health':ti,ab,kw OR ehealth:ti,ab,kw OR telemonitoring:ti,ab,kw OR telementoring:ti,ab,kw OR teleassistance:ti,ab,kw OR 'tele assistance':ti,ab,kw) AND [2019-2020]/py #3- #1 AND #2	46
Open Grey	("Oral Oncology" OR "Head and Neck Oncology" OR "Mouth Neoplasms" OR "Mouth Neoplasm" OR "Neoplasm, Mouth" OR "Neoplasms, Oral" OR "Neoplasm, Oral" OR "Oral Neoplasm" OR "Oral Neoplasms" OR "Neoplasms, Mouth" OR "Cancer of Mouth" OR "Mouth Cancers" OR "Oral Cancer" OR "Cancer, Oral" OR "Cancers, Oral" OR "Oral Cancers" OR "Cancer of the Mouth" OR "Mouth Cancer" OR "Cancer, Mouth" OR "Cancers, Mouth" OR "Head and Neck Neoplasms" OR "Neoplasms, Head and Neck" OR "Head, Neck Neoplasms" OR "Cancer of Head and Neck" OR "Head and Neck Cancer" OR "Cancer of the Head and Neck" OR "Upper Aerodigestive Tract Neoplasms" OR "UADT Neoplasms" OR "Neoplasms, UADT" OR "Head Neoplasms" OR "Neoplasms, Head" OR "Neck Neoplasms" OR "Neoplasms, Neck" OR "Cancer of Head" OR "Head Cancer" OR "Cancer of the Head" OR "Cancer of Neck" OR "Neck Cancer" OR "Cancer of the Neck" OR "Malignant Disorders" OR "Precancerous Conditions" OR Premalignant OR Premalign OR Premalignancies OR Premalignancy) AND (Teledentistry OR Tele-dentistry OR Tele-triage OR Teletriage OR Triaging OR Telemedicine OR Tele-medicine OR "Mobile Health" OR "Health, Mobile" OR "Mhealth" OR Telehealth OR Tele-health OR Ehealth OR Telemonitoring OR Telementoring OR Teleassistance OR Tele-assistance)	0
Google Scholar	With all words ("Oral Oncology" OR "Oral Cancer" OR "Head and Neck Neoplasms" OR "Cancer of the Head and Neck") AND (Teledentistry OR Telemedicine OR Telehealth) Date: 2019-2020	100
JSTOR	(("Oral Oncology" OR "Oral Cancer" OR "Head and Neck Neoplasms" OR "Cancer of the Head and Neck") AND (Teledentistry OR Telemedicine OR Telehealth)) Publication Date: From 2019 to 2020	0 *(continued)*

Appendix 2 - Excluded articles and reasons for exclusion (n=12).

Author, year	Reasons for exclusions
Capocasale G (1), 2020	07
Ghai S. (2), 2020	08
Graboyes E et al. (3), 2020	09
Huang VW. (4), 2020	08
Machado RA. (5), 2020	04
Mannelli G (6), 2020	09
Motta ACF (7), 2020	07
Patel T. (8), 2020	04
Prasad A. (9), 2020	08
Ratnasekera N. (10), 2020	08
Singh AG. (11), 2020	09
Triantafillou V. (12), 2020	08

1 - In vitro studies; 2 - Studies of animal models; 3 - Guidelines, abstracts, book chapters, research protocols and posters; 4 - Studies evaluating other medical/dental specialties; 5 - Studies with telemonitoring of other types of primaries cancer; 6 - Telemonitoring's studies of other comorbidities (cardiovascular, conditions, heart failure, Chronic Obstructive Pulmonary Disease, HIV/AIDS, obstetric disease, Asthma, hypertension, diabetes, obesity hepatitis C, mental illness , nephrotic diseases etc); 7 - Studies evaluating the use of teledentistry for telediagnostics; 8- Monitoring of oral and head and neck cancers performed by other professionals (otolaryngologists, nurses, etc.); 09 - Studies evaluating oral cancer or head and neck cancer with subjects unrelated to teledentristy;

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11. Singh AG, Deodhar J, Chaturvedi P (2020) Navigating the impact of COVID-19 on palliative care for head and neck cancer. Head Neck. 42(6):1144-1146 doi: 10.1002/hed.26211
12. Triantafillou V, Rajasekaran K. (2020) A Commentary on the Challenges of Telemedicine for Head and Neck Oncologic Patients during COVID-19. Otolaryngol Head Neck Surg 163(1):81-82 doi: 10.1177/0194599820923622

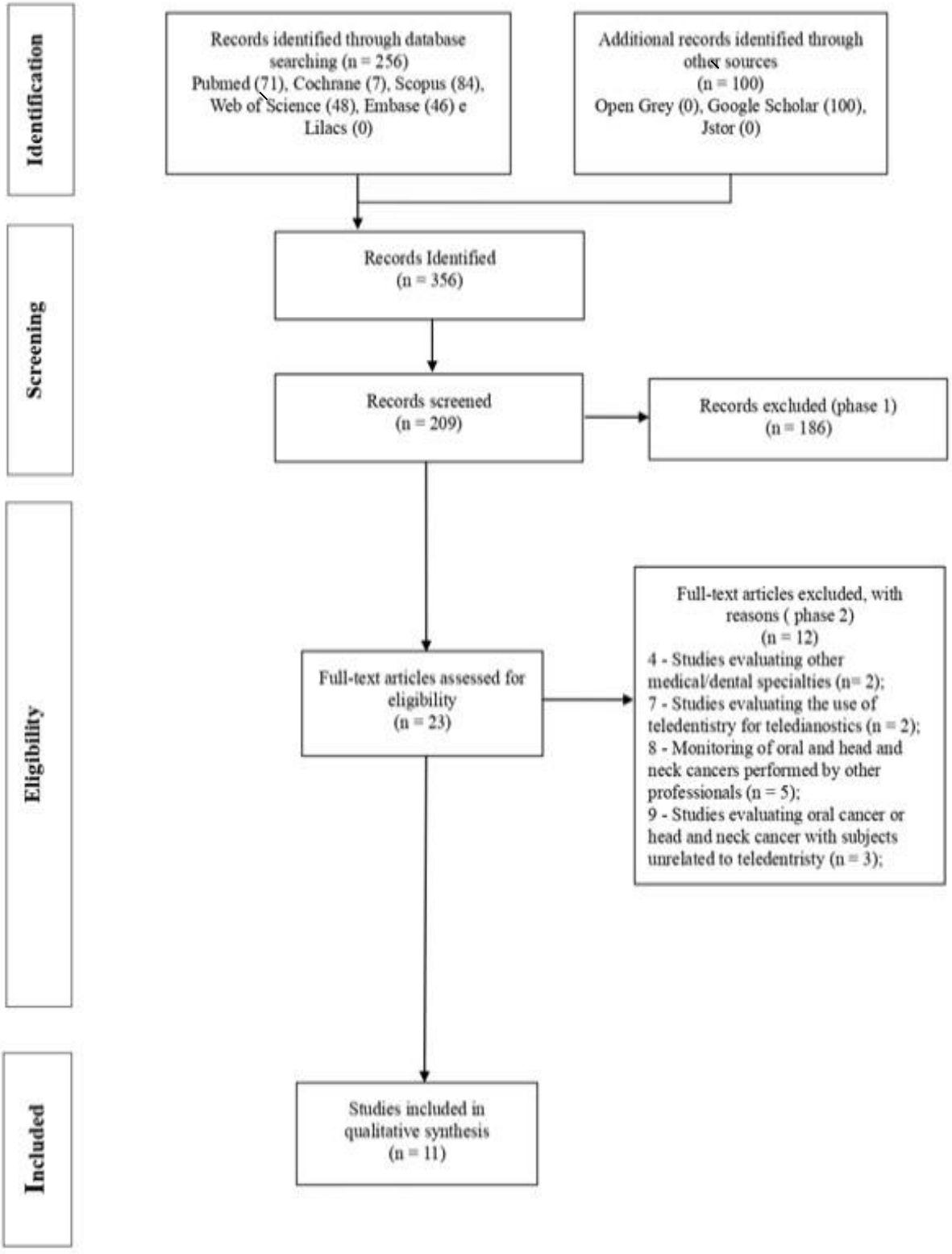

Figure 1 - Flow diagram of the integrative review

Table 1 - Summary of descriptive characteristics of included articles (n=11).

Author, year, country	Characteristics of users and/or professionals who use remote technology (n)	Security criteria required by remote technology	Remote Technology used or deployed	Description of the use of the remote technology adopted and evidence of management, control and assistance by teledentistry	Main Conclusions
Al-Maweri SA, 2020, Saudi Arabia	Patients already diagnosed with oral potentially malignant disorders (n)	-------	Zoom, Messenger, and Facebook	• Scheduling, interview, do clinical examination, and even to conduct oral habits cessation counseling for their patients • Patients can take photographs of their mouths and send them to the dentists at regular intervals Virtual education regarding clinical signs and risk factors of oral cancer	During a pandemic other important health issues may be neglected by the public and ignored by the health systems and the dental profession has a role to engage in managing serious health issues such as “detecting oral cancers early” as an ethical responsibility.

Table 1 (continued)

Author, year, country	Characteristics of users and/or professionals who use remote technology (n)	Security criteria required by remote technology	Remote Technology used or deployed	Description of the use of the remote technology adopted and evidence of management, control and assistance by teledentistry	Main Conclusions
Alves FA, 2020, Brazil	Patients who are undergoing oncological treatment (n)	-------	-------	• Virtual visits have greatly facilitated the provision of oral medicine care and support for both established and new consultations, allowing for effective triage of potentially urgent cases problems requiring immediate clinical attention • Telemedicine/dentistry or telehealth is used to facilitate patient–professional communication and is widely and effectively incorporated into oncology care	In summary, our group has demonstrated various strategies, often coordinated at the institutional level, to maintain essential oral/dental care for cancer patients during the COVID-19 pandemic. We anticipate that there will be many lessons learned from this experience that will have the potential to improve access to oral medicine care for cancer patients in the future.
Kanatas A & Rogers SN, 2020, England	not reported	-------	Remote telephone consultations accompanied by a questionnaire (PCI-HN)	There is potential merit for members of the head and neck team in using the PCI-HN as part of a telephone review consultation. This would serve to help standardize and guide the consultation, aid multi-professional communication, and avoid missing key issues.	The PCI-HN may provide a very useful tool to aid remote consultations, but more clinical evidence is needed in order to ensure that such consultations are optimal for our head and neck patients.

Table 1 (continued)

Author, year, country	Characteristics of users and/or professionals who use remote technology (n)	Security criteria required by remote technology	Remote Technology used or deployed	Description of the use of the remote technology adopted and evidence of management, control and assistance by teledentistry	Main Conclusions
Barca I et al., 2020, Italy	Cancer Patients (54 males, 36 females ratio - 1.5:1). Range age overall - 17 to 95 mean age - 62.15 years. 37 - resident in Catanzaro 53 - from other provinces of Calabria	Data sent to the examiner's smartphone using WhatsApp application that uses end-to-end encryption, so the communication by phone is secure. The phone to the photos were sent was only accessible to a small group of professionals through the use of specific authentication credentials. The conservation, transmission and use of patient data were in compliance with the ethical and legal responsibilities of confidentiality and professional secrecy, in full compliance with the General Data Protection Regulation (GDPR)	WhatsApp or Telegram applications that use end-to-end encryption for telephone messaging. The photos taken by the patient or with the help of a direct relative to acquire the following images: (1) a photo of the face and/or neck; (2) a photo of the oral cavity; (3) a photo of the maximum buccal opening with a visible millimeter ruler.	A Group For subgroup A1 the evaluation was carried out through CD visualization, photos taken by the patient or a family member, evaluation of symptoms. For subgroup A2 was considered signs of deterioration through the modification of the tissue morphological characteristics; MRONJ -variation of the stage and the presence of infection signs were assessed. B Group For both subgroups, the evaluation of the clinical picture was conducted both through the video call, the evaluation of the clinical photos sent and through the display of symptoms. Questionnaire of satisfaction 73% found it easy to participate in the consultation, 20% moderate and 7% difficult. 78% prefer telemedicine today, 12% indigenous and 10% face to face consultation 80% chose the video-phone consultation over the telephone consultation. 92% would recommend video calling to others.	Telemedicine represents an excellent opportunity to improve accessibility to oncological and non-oncological treatments. Telemedicine is indicated above all in the follow-up of cancer patients, because they are immunosuppressed for previous chemo/radiation treatments and therefore subject to greater risk of contagion, in chronic as well as urgent visits for suspected malignancy and in patients who live far from a hospital.

Table 1 (continued)

Author, year, country	Characteristics of users and/or professionals who use remote technology (n)	Security criteria required by remote technology	Remote Technology used or deployed	Description of the use of the remote technology adopted and evidence of management, control and assistance by teledentistry	Main Conclusions
Crispo A et al, 2020, Italy	Cancer patients in IRCCS Fondazione G. Pascale (n)	-------	E-mail for tests results; careful telephone monitoring symptoms.	• Establishment of waiting rooms for cancer patients Implementation of active surveillance to identify cases earlier, isolating them according to appropriate management and containment procedures • Visits of cancer patients treated with oral anticancer drugs are performed telematically • The first non-urgent visits have been postponed, for fear of contagion by COVID-19 infection • Use of telemedicine as tools in order to plan for personnel, including patient count, a definition of patients who may benefit from this approach and useful to cancer screening programs	The follow-up of outpatients with telemedicine should be individualized and based on disease severity and initial treatment priorities. In this pandemic situation a multidisciplinary approach for the management of cancer patients should be improved where possible in order to give the most priority to patients, better equilibrating oncologic and COVID-19 needs.

Table 1 (continued)

Author, year, country	Characteristics of users and/or professionals who use remote technology (n)	Security criteria required by remote technology	Remote Technology used or deployed	Description of the use of the remote technology adopted and evidence of management, control and assistance by teledentistry	Main Conclusions
Kang JJ, et al, 2020, EUA	Cancer patients in Memorial Sloan Kettering Cancer Center (n)	-------	Multidisciplinary Visits used the Zoom app	• Radiation department has stopped all endoscopic procedures. Use of PET, CT and/or magnetic resonance imaging—for radiation planning • No elective dental extractions before radiation • Nonsurgical management is preferred when surgery and Radiation Treatment have equal outcomes • Urgent essential cases may proceed after a rigorous preoperative review and negative preoperative COVID-19 testing. Patients who test positive - reassessed for surgery at a later date • An official swab test is performed, and if it is positive - stop treatment for 10 days and resume treatment if asymptomatic • Patients grateful for telemedicine visits, and no telemedicine-consultation, status-check, or follow-up patients has been requested an in-person visit • The communication with multidisciplinary colleagues by Zoom app is to anticipate barriers, prepare contingency plans, evaluate their efficacy, and refine/revise operations	With the current global magnitude of the crisis and the immediate challenges of testing and PPE shortages in the United States, telemedicine has been the backbone of our strategy to protect against infection and continue the fight against cancer.
Lopes MA, 2020, Brazil	not reported	-------	-------	• Telemedicine is used in remote areas where adequate structure to treat patients is lacking. Is an alternative not only for patient education but also to contribute to diagnosis, and treatment • Results of clinical imaging, radiography, CT, histopathology and tumor board conferences can be verified via telemedicine • Virtual assistance to patients with cancer and to health care professionals, particularly dentists, help prioritize higher-risk cases, while avoiding face-to-face contact. Only patients with highly suspicious malignant lesions would be referred to the oral medicine team for clinical examination and procedures.	Telemedicine in oral medicine has potential to support clinicians and patients and contribute to reducing unnecessary hospital visits and help preserve the resources for those who need them the most.

Table 1 (continued)

Author, year, country	Characteristics of users and/or professionals who use remote technology (n)	Security criteria required by remote technology	Remote Technology used or deployed	Description of the use of the remote technology adopted and evidence of management, control and assistance by teledentistry	Main Conclusions
Kochhar AS, 2020, India	not reported	-------	Dentists can provide support to patients undergoing radio and/or chemotherapy via telephone and where possible video calls	• Dentists must motivate and re-emphasize oral hygiene measures • Informations about what to anticipate during oncology treatment (such as mucositis, xerostomia and possible dysgeusia), and actions to extenuate these effects • Counsellation about the teeth mineralization before oral hygiene maneuvers become to discomfort and the risk of caries that arises due to dry mouth • The importance of long-term follow-up, especially due caries and osteoradionecrosis. Dental practitioners can request photographs or radiographs in diagnosis and advise home care measures • Constant check-ups, counselling and support via tele-dentistry consultations to maintain and improve overall well-being of the patients and consequently, QOL	It is imperative to provide continuous dental care to oral cancer patients, and dentists must ensure that there is no hindrance to the same, while reconsidering traditional treatments in light of the prodigious situation presented by the COVID-19 pandemic, in liaison with the oncologist.

Table 1 (continued)

Author, year, country	Characteristics of users and/or professionals who use remote technology (n)	Security criteria required by remote technology	Remote Technology used or deployed	Description of the use of the remote technology adopted and evidence of management, control and assistance by teledentistry	Main Conclusions
Lee AKF et al., 2020, Hong Kong	Cancer patients in United Christian Hospital and Tseung Kwan O Hospital	The Information Technology Department of the Hospital Authority recommended to use the latest version of the Zoom client with a corporate account to enjoy enterprise security features. A password should be set for every meeting and the meeting details and password should be exclusively disclosed to participants only. The “Lock” function should be enabled the meeting to avoid intrusion.	To accomplish the telemedical sessions, Zoom was adopted Two sessions per week for doctor with six consultations per session. Telemedicine sessions -10 minutes longer when compared with a face-to-face consultation of usually less than 10 minutes per patient.	• Telemedicine is utilized to reduce patient's travel and hospital attendance to minimize the risk of cross infection • Telemedicine can provide preoperative counseling, education on postoperative care, dietary advice and exercise recommendations for neck and shoulders. In the postoperative phase: simple wound review and troubleshooting PPE: personnel were kept to a minimum perioperatively for intubation and extubation and for airway operations to reduce contact and conserve PPE • The distribution of priority patients with head and neck cancer between regional ENT units to provide timely surgery Tumors with more aggressive clinical behavior, high tumor volume and rapid disease progression was prioritized due the possibility progression to airway obstruction requiring an emergency tracheostomy, metastases and higher morbidity and prolonged hospital stay for the patient	Since the initiation of this multi-institutional collaboration, it has been able to alleviate the number of pending head and neck cancer operations by 20%. Novel methods such as telemedicine and regional collaboration with other centers have been implemented with some success, with plans for further development in the coming months.

Table 1 (continued)

Author, year, country	Characteristics of users and/or professionals who use remote technology (n)	Security criteria required by remote technology	Remote Technology used or deployed	Description of the use of the remote technology adopted and evidence of management, control and assistance by teledentistry	Main Conclusions
Meurer MI, 2020, Brazil	The State of Santa Catarina has 39 registered oral medicine (OM) specialists (one per 183,700 inhabitants)	The tele(oral)medicine module was implemented in the STT/SC web-based system, complying with the security criteria, according to the Brazilian regulations (i.e., confidentiality/encryption, authenticity, integrity, irrefutability and timestamping).	The Santa Catarina State Integrated STT/SC offers coverage to 100% of the municipalities, and it integrates primary, secondary and tertiary healthcare facilities in a single infrastructure. Tele(oral)medicine module aggregates a set of functionalities: (a) the collection of clinical data by the dentist at the primary health units, (b) the remote support by a specialist to manage clinical conditions that can be treated at primary healthcare units and (c) the proper referral of patients to secondary health units.	Dentists at primary healthcare units collect clinical data and images of oral lesions, registering the information via STT/SC portal. The OM specialist then evaluates the case and provides a report, indicating the clinical management. When a more serious condition is suspected, an urgency priority is established and face-to-face consultation at a secondary healthcare unit is authorized. Elective cases, during the pandemic, are being monitored at primary healthcare units and being placed on a waiting list.	The telemedicine/telehealth tools are useful to provide clinical and supportive care to patients with oral diseases in these pandemic times. We also believe in the educational potential of the relationships established between professionals through the referral processes of patients, even if they are mediated by interactions at a distance.

Table 1 (continued)

Author, year, country	Characteristics of users and/or professionals who use remote technology (n)	Security criteria required by remote technology	Remote Technology used or deployed	Description of the use of the remote technology adopted and evidence of management, control and assistance by teledentistry	Main Conclusions
Shanti RM et al, 2020, EUA	not reported	-------	BlueJeans (Mountain View, California) and Doximity (San Francisco, California) as video conferencing platforms.	• Acquisition of medical and dental records: clinical photographs, photographs provided by the patient of the lesion(s); copy of biopsy report(s) •Telehealth consultation: a spatial appreciation of a lesion is achieved and better assessment for cervical lymphadenopathy through video, which adds a degree of human touch to the visit •Determine urgency/timing of in-person visit: our rational for the use of the 3-month time point in low-risk lesions is based on literature •PPE patient SARS-CoV-2 negative: level 3 surgical mask with face shield and/or goggles during the in-person evaluation – Patient untested or surgical procedure: N95, face shield, disposable medical safety gown, and disposable working cap • SARS-CoV-2 testing: With regard to testing stewardship, Telehealth evaluation allows for optimization of the efficiency of the in-person visit, evaluate any medications, conditions specials or obtaining any necessary “clearances” •Topical preparation of oral mucosal surfaces with povidone-iodine (PVP-I): the use PVP-I (1%-7.5%) for 2 minutes to inactive SARS coronavirus •Technical considerations for tissue handling: use of either a surgical scalpel or a tissue biopsy technique with avoidance of use of laser due to viral transmission by laser-generated plume, use of absorbable sutures and minimize use of smoking-generating cautery to diminish vaporization of viral particles •Procedure setting: the procedure can be performed in the outpatient clinic setting or in the operating room depending on the status of the SARS-CoV-2 tests, and whether the lesion is easy or difficult to access	The COVID-19 pandemic has required health care practitioners to make novel decisions that are new to us with development of creative pathways of care that focused on patient safety, mitigation efforts, and clinical management of disease processes. The care of patients with OPMDs requires special considerations especially as patients at high risk for severe COVID-19 illness are also higher risk for the development of OPMDs.

Subtitles: STT/SC = Telemedicine and Telehealth System; OC = Oral Cancer; HNC = Head Neck Cancer; PCI-HN = Patient Concerns Inventory – Head and Neck; IRCCS = Istituto di Ricovero e Cura a Carattere Scientifico QOL = Quality of life; MRONJ = Medication-Related Osteonecrosis of the Jaws; PPE = personal protective equipment; CT = computed tomography; PET = positron emission tomography; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; PVP-I = povidone-iodine; OPMD= oral potentially malignant disorders;

Table 1 - Benefits of using teledentistry in select studies

Thematic cathegory	Evidence of the benefits of using teledentistry
Virtual visits	- Allow to monitor the use of medications reducing patient's hospital attendance to minimize the risk of cross infection [34,37]. - Provide preoperative counseling, education on postoperative care, dietary advice and exercise recommendations for neck and shoulders. In the postoperative phase: simple wound review and troubleshooting [34,37]. - Provide oral medicine care to potentially urgent cases with highly suspected malignant lesions[35,36]. - Allow follow-up, interviews, clinical examinations with the guidance of oral habits, control of the virtual education of the patients about the clinical signs and risk factors of oral cancer, reduces anxiety with information available in the common media and permit a spatial appreciation of a lesion through video for their patients [4,36,40]. - Promote better patient-professional communication before, during and after cancer care to maintain and improve patient's quality of life [35,36]. - Management by the dentist of the evolution of the lesions through the use of photographs and copies of the biopsy reports of the mouth sent by the patients in virtual consultations [33].
Use of remote technology	- Teledentistry are used to evaluate results of clinical imaging, radiography, computed tomography, histopathology tests and carry out tumor board conferences [39]. - Teledentistry for patients with cancer and to health care professionals, particularly dentists, help prioritize higher-risk cases, while avoiding face-to-face contact [39]. - The use of telephone associated or not with a structured guide, video conference applications like Zoom app and TD's integrated models to increase the coverage of oral oncology services used for TD's consultations [31,32,34].
Patient´s satisfaction	- High rate of patient's satisfaction with the use of teledentistry with 98% ease of use, with the use of video phones being chosen by 98% of patients and 92% would recommend video calling to others [33,38]. - Patients grateful for TD's visits, and no TD's consultation has requested a visit in person for status verification or follow-up [33,38].
Multidisciplinary approach in teledentistry	- Multidisciplinary action throught the collaboration between different regional units to provide timely surgery was made possible, optimizing treatment during the pandemic [34,38, 37]. - Communication with colleagues in a multidisciplinary way throught Multidisciplinary tumor councils, academic meetings or multidisciplinary tumor board meetings via applications such as Zoom [34].

Table 2 - Evaluation of methodological quality according to the design of the study (n=11)

Study	Methodological quality assessed								Total (% score yes)	Methodological quality
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8		
Barca I (2020)	Y	N	Y	Y	Y	U	Y	Y	75%	High
Kang JJ, et al (2020)	N	N	N	Y	Y	Y	Y	Y	62,50%	Moderate
Lee AKF (2020)	Y	N	Y	Y	Y	N	Y	Y	75%	High
Shanti RM et al (2020)	N	N	Y	U	Y	N	N	Y	37,50%	Low
Al-Maweri SA (2020)	Y	Y	Y	Y	Y	N	--	--	83,33%	High
Alves FA (2020)	Y	Y	Y	Y	Y	N	--	--	83,33%	High
Crispo A et al (2020)	Y	Y	Y	Y	Y	N	--	--	83,33%	High
Kanatas A (2020)	Y	Y	Y	Y	Y	N	--	--	83,33%	High
Kochhar AS (2020)	Y	Y	Y	Y	Y	N	--	--	83,33%	High
Lopes MA (2020)	Y	Y	Y	Y	Y	N	--	--	83,33%	High
Meurer MI (2020)	Y	Y	Y	Y	Y	N	--	--	83,33%	High

Note: For Case Reports - Q1. Were patient's demographic characteristics clearly described? Q2. Was the patient's history clearly described and presented as a timeline? Q3. Was the current clinical condition of the patient on presentation clearly described? Q4. Were diagnostic tests or assessment methods and the results clearly described? Q5. Was the intervention(s) or treatment procedure(s) clearly described? Q6. Was the post-intervention clinical condition clearly described? Q7. Were adverse events (harms) or unanticipated events identified and described? Q8. Does the case report provide takeaway lessons?
For Text and Opinion - Q1. Is the source of the opinion clearly identified? Q2. Does the source of opinion have standing in the field of expertise? Q3. Are the interests of the relevant population the central focus of the opinion? Q4. Is the stated position the result of an analytical process, and is there logic in the opinion expressed? Q5. Is there reference to the extant literature? Q6. Is any incongruence with the literature/sources logically defended?

Abbreviations: N, no; U, unclear; Y, yes

CAPÍTULO 3 - THE FEASIBILITY OF TELEHEALTH IN THE MONITORING OF HEAD AND NECK CANCER PATIENTS: A SYSTEMATIC REVIEW ON REMOTE TECHNOLOGY, USER ADHERENCE, USER SATISFACTION, AND QUALITY OF LIFE

da Silva HEC, Santos GNM, Ferreira Leite A, Mesquita CRM, de Souza Figueiredo PT, Miron Stefani C, de Santos Melo N. The feasibility of telehealth in the monitoring of head and neck cancer patients: a systematic review on remote technology, user adherence, user satisfaction, and quality of life. Support Care Cancer. 2022 (10):8391-404. doi: 10.1007/s00520-022-07109-z.

3.1 ABSTRACT

Objectives: This systematic review aimed to analyze the use of telehealth in monitoring patients with head and neck cancer regarding the application used, user adherence to technology, user satisfaction, and user quality of life.
Materials and Methods: A search strategy was developed using the PICO acronym and the terms “Head and Neck Cancer”, “Telehealth”, “Mobile Application” and “Supportive Care”. A broad literature search was performed on PubMed, Cochrane Library, Scopus, Web of Science, Lilacs, Embase databases and on grey literature through Open Grey, Google Scholar, and Jstor, for studies comparing the monitoring of head and neck cancer patients with telehealth apps to the monitoring performed in a traditional way at health units. No study design, publication status, publication time or language restrictions were applied. Pairs of reviewers worked independently for study selection and risk of bias assessment. The protocol was registered in PROSPERO and the PRISMA checklist used for reporting the review.
Results: We found 393 references in the databases, 325 after duplicates removal, 19 met the criteria for full-text reading, 08 studies were included for qualitative synthesis. Although there was heterogeneity regarding the technology used, the studies included showed that remote monitoring and/or self-management of symptoms through mobile applications was feasible for most patients, with satisfactory degrees of acceptability, satisfaction, usability and adherence. The health-related quality of life improved with the use of remote technologies for telehealth, associated with low to moderate self-efficacy, higher personal control, and higher knowledge of health with clinically acceptable levels of accuracy compared to traditional clinical evaluation. Even when the data presented were not statistically significant, patients reported improvement in health-related quality of life after the intervention.
Conclusions: Telehealth monitoring through the use of remote technologies presents itself as an alternative way for educating and supporting patients during the treatment of Head and Neck Cancer (HNC). There is the need for a more user-friendly interface, adequate user experience assessment, and the concrete applicability of telehealth technologies for monitoring patients with HNC in order to legitimize the cost-effectiveness of developing long-term multicenter longitudinal studies term.
Keywords: Telehealth, Oral Cancer, Head and Neck Cancer, Monitoring, Systematic Review.

3.2 INTRODUCTION

Patients undergoing treatment for head and neck cancer (HNC) encounter numerous challenges due to their diagnosis and treatment. Despite advances in these areas and in management, treating HNC often entails considerable functional impairment including not only acute, but long-term chronic changes that impact swallowing, eating, periodontal health and oral care, speech, and social functioning [1,2]. As a result, daily routine activities can become more challenging [3,4].

Treatment for HNC is most often a rigorous regimen of combined therapies producing a multitude of distressing symptoms and side effects. While it is nearly impossible to circumvent the insults caused by such treatment, interventions in treating addictions such as alcohol and tobacco, psychological and social support groups comprised of family, friends, and neighbours, directed towards educating and sustaining patients during active treatment, have been successful [5,6].

Cancer and its treatment have a major impact on a survivor's quality of life (QOL). Symptoms such as fatigue, oral dysfunction, speech and swallowing problems, and related social withdrawal and psychological distress can deteriorate QOL [7] and increase survivors' needs for supportive care services. Previous QOL research in this population has consistently demonstrated a deterioration in QOL during the first three months of the treatment, followed by a slow recovery [8].

In this context, eHealth self-management interventions may positively affect health-related quality of life (HRQOL) and symptom burden among cancer survivors, but effect levels vary considerably [9,10]. Most are adjunctive or guided behavioral intervention technologies, and a healthcare provider is needed to discuss the results and the supportive care options that best fit the patient's needs. Online self-management interventions can have positive effects on HRQOL and symptom burden in patients with cancer [11,12].

Remote medicine allowed new approaches to communication between physicians and patients during the treatment of chronic and acute diseases, improving patient education, support, and diagnostic [13]. In addition, telephone-based systems have been used to report and monitor cancer symptoms with favorable compliance noted even when patients are expected to initiate calls on a regular basis [14,15]. Favorable acceptance ratings have also been reported by both

patients and clinicians regarding computerized systems used to assess symptoms and quality of life in cancer patients [16 -18].

With the rising popularity of smart devices, such as cell phones and tablets, the use of mHealth applications (apps) has increased in many countries [19]. These apps transmit medical information quickly and efficiently, as well as provide health services to patients. Several mHealth apps have been developed for disease management approaches such as blood glucosecontrol (diabetes) [20], hypertension control [21], depression treatment [22], remote cancer surveillance [23], and medication monitoring [24].

Consequently, supportive cancer care innovation includes the incorporation of self-management and eHealth, implementation of evidence-based approaches to monitor QOL [25], and the redesign of the organization of supportive care according to participant-centered models (e.g., the chronic care model, disease management, and stepped care) [26].

Hence, the main objective of this systematic review was to analyze the use of telehealth (TH) in monitoring patients with head and neck cancer regarding the model of technology used, user adherence to technology, user satisfaction and quality of life. The focused question was: “What are the degrees of adherence of users, user satisfaction and quality of life with the adoption of telehealth for monitoring the treatment of patients with head and neck cancer?”

3.3 METHODS

Protocol Registration

The protocol of this study was registered on the International Prospective Register of Systematic Reviews - PROSPERO (www.crd.york.ac.uk/PROSPERO/) under number CRD42021233292 and Protocols.io register: dx.doi.org/10.17504/protocols.io.bvv9n696. This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses, following the PRISMA checklist (http://www.prisma-statement.org/).

Search Strategy

On January 21st, 2021, it was performed a broad search of articles without language or time limits in the following databases: PubMed, Cochrane Library, Scopus, Web of Science, Lilacs (Latin American and Caribbean Literature), Embase, and grey literature through Open Grey, Google Scholar, and JSTOR. The Medical Subject Headings (MeSH) terms “Head and Neck Cancer”, “Telehealth”, “Mobile Application”, “Supportive Care” and synonyms were used to develop the search strategy (available in Additional file 1) and to acquire the main one on PubMed. When words with different spelling appeared, synonyms present in the MeSH terms were used. This strategy was adapted for the other databases. Manual searches of reference lists of relevant articles were also performed.

Immediately after the literature search, the references were exported to the reference manager online Rayyan QCRI (https://rayyan.qcri.org/welcome) and duplicated references were removed.

Inclusion And Exclusion Criteria

PICO (Population, Intervention, Comparison, and Outcomes) research strategy was used to define the inclusion and exclusion criteria. As inclusion criteria, studies monitoring oral and head and neck cancer patients (P) with TH apps (I) compared to the monitoring performed by the traditional treatment (C) at health units. The technology tool model for TH used, the number of patients adhering to the technology tool, patient and professional satisfaction with the technology tool were the primary outcomes considered (O).

Exclusion criteria comprised: 1- Reviews, editorials, letters, conferences, summaries, opinions, abstracts, and posters; 2- *In vitro* studies and studies in animal models; 3 - Qualitative studies; 4 - Thesis and Dissertations and book chapters; 5 - Pipelines, guidelines, and research protocols; 6 - Studies not using remote technologies; 7- Studies evaluating other medical/dental specialties; 8 - Studies telemonitoring other types of cancer; 9 - Studies telemonitoring other

diseases/conditions (heart failure, Chronic Obstructive Pulmonary Disease, HIV, obstetric disease, Asthma, hypertension, diabetes, *etc*.); 10 - Studies using remote technologies for improvement of knowledge among health professionals (caregivers, nurses, doctors, *etc*.); 11 - Studies using remote technologies to assess behavioral, emotional, and cognitive aspects.

Study Selection

The studies selection took two phases. In phase 1, two independent reviewers (HECS and GNMS) evaluated the titles and abstracts of all records according to the eligibility criteria. In phase 2, both reviewers (HECS and GNMS) independently read the full texts according to the inclusion and exclusion criteria. In case of disagreements, both reviewers discussed and, if consensus was not reached, a third reviewer (AFL) was consulted to reach a final decision.

Data Extraction

Data extraction was also carried out by two independent reviewers (HECS and GNMS) and cross-checked. Extracted data comprised author, year, country, sample, age in years (mean± SD and/or range); groups (n and treatments); Technology tool model for TH used; Number of patients adherering to the use of the technology tool; Patient satisfaction using the technology tool and quality of life (P-value); and the main conclusions of each paper. When necessary, a request for additional information was made to the authors of the selected articles via e-mail.

Methodological quality assessment

The JBI Critical Appraisal Tools (Joanna Briggs Institute, 2014) were used to

assess the methodological quality of the studies independently by two reviewers (HECS and GNMS), accordingly to the design of the included studies, namely: JBI critical appraisal checklist for Randomized Controlled Trials (RCTs) and JBI critical appraisal checklist for Quasi-experimental Studies [27]. The purpose of this appraisal was to determine the extent to which it has addressed the possibility of bias in its design, conduct, and analysis. This methodological quality assessmentcould then be used to inform the synthesis and interpretation of the results of the study [27].

Studies were characterized according to the scoring decisions agreed by reviewers previously. For RCTs, low-quality: 1 to 5 “yes” answers; moderate-quality: 6 to 10 “yes” answers; high-quality: 11 to 13 “yes” answers. For Quasi-experimental studies: low-quality: 1 to 3 “yes” answers; moderate-quality: 4 to 6 “yes” answers; high-quality: 7 to 9 “yes” answers.

Considered Outcomes

The intervention effects were compared to the following outcomes: technology tool model for TH used, number of patients who adhere to the use of the technology tool, patient satisfaction with the use of the technology tool, and quality of life. Despite a meta-analysis had been planned, the results showed high methodological heterogeneity, turning it to be unfeasible.

3.4 RESULTS

Description Of Included Studies

The electronic research in five databases resulted in 393 records. Removal of duplicated studies resulted in 68 records. Titles and abstracts from these studies were read and those not fulfilling the eligibility criteria were excluded. In addition, grey

literature was searched. JSTOR and Open Grey returned 0 references. All 240 references from Google Scholar were consideredfor evaluation. At the end of phase 1, 19 studies remained for full-text reading (phase 2). A manual search of reference lists did not provide additional studies. Full-text reading resulted in eight eligible studies for qualitative analysis. Additional file 2 presents excluded articles and the reasons behind removals. Finally, the flowchart of the complete inclusion process is shown in Figure 1.

Figure 1 should be placed here.

Included studies were conducted in EUA [28,29,13], Netherlands [30,31,32], Italy [33], and Taiwan [34]. All included studies were published in English. Three selected studies were RCTs [29,13,31], one was a cross-sectional study [33] and four were Quasi-experimental studies [28,30,32,34]. The application of remote technologies in the monitoring of patients with Oral Cancer (OC) and HNC was evaluated according to the percentage of user adherence, user satisfaction, and quality of life.

Table 1 summarizes details of studies regarding population, interventions, outcomes, and conclusions.

Table 1 should be placed here.

Methodological quality within studies

None of the studies fulfilled all methodological quality criteria. However, four studies [28,30,33,34] were considered of high methodological quality, three studies [29,31,32] were of moderate methodological quality, and only one study [13] was considered of low methodological quality.

In studies [29,13,31], assessed with JBI's checklist for RCT, patients, those who administered the treatment, and the outcome assessors were not blind to the treatment's assignment. Two studies [29,13] did not show randomization and adequate concealed allocation of participants to treatment groups.

In studies [28,30,32,33,34], assessed with JBI's checklist for Quasi-experimental studies, the participants were not included in any comparisons receiving similar treatment/care other than the exposure or intervention of interest.

Three studies [28,30,33] did not present a control group, one study [32] did not describe and analyze differences between groups in terms of their follow-up, in one study [31] outcomes were not measured reliably and in one study [33] the participants were not included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest.

More information about the methodological quality can be found in Table 2 andTable 3 (summarized assessment).

Table 2 and Table 3 should be placed here.

Results Of Individual Studies

In the study carried out in Milan, Italy [33], ten patients and three physicians used the "HeNeA" app for a 65-days-period and were evaluated through a questionnaire on satisfaction with the app. The mean score per patient was 18.5 (interquartile range 11.2–20.5) and 16 (range 11–20) per physician, with overall positive satisfaction with the use of the app. Perceived usefulness and usability had a positive correlation and were considered independent predictors of acceptance. However, the study showed a significant negative correlation ($\beta = -0.0249$, $p = 0.007$) between reported symptom severity and EuroQoL questionnaire scores. The study showed that symptom monitoring in patients with HNC through a cell phone app was feasible and acceptable for patients and oncologists, although the results could not be generalized or compared to other methods due to the small sample size.

Another study conducted in Philadelphia, USA [28] used the web-based program "My Journey Ahead" in order to provide the patient with information and methods of self-management of concerns related to HNC symptoms. Acceptance and satisfaction were assessed in 55 enrolled patients by using the program. Evaluations were carried out before and after the use of "My Journey Ahead", where the evaluated criteria were measures of psychological distress, self-efficacy in dealing with issues related to cancer, and satisfaction with the use of the website. Forty-four patients (80%) logged in and viewed the web-based program. The program was considered interesting and easy to use, and high levels of patient

satisfaction were reported. Satisfaction levels were related mainly to older age and self-efficacy in fighting cancer. The authors considered the application useful in coping with and understanding the HNC. In a Quasi-experimental study conducted in New Taipei City, Taiwan [34], a mobile Health (mHealth) app has enabled changes in the assessment of care needs of oral cancer patients, improving their quality of life. One hundred patients were divided into a test group (n =50) that used the mHealth intervention and into a control group (n = 50) that received traditional health care.

The evaluation period was three months, with the use of survey questionnaires to verify the quality of life of patients, nursing care needs, and acceptance of the use of the mHealth intervention. The patients from the test group showed a decrease in physiological care needs ($P < 0.05$). On the other hand, psychological, communication, and care support needs were not different between groups, although improvements with the use of the mHealth intervention were reported. Despite greater improvement in quality of life was observed for patients in the test group compared to the control group (-7.24 vs. -4.36), no statistical significance was found. The study reported a reduction in the need for nursing care using the mHealth intervention. In addition, users improved their quality of life and their level of acceptance of the app, although the data only allowed for speculative and biased analysesdue to the low statistical significance of the evaluated results.

Two RCTs studies were conducted in Louisville, Kentucky, USA. The first compared the TH intervention using the “Health Buddy®” system to standard care [13]. The other evaluated the impact of the “Health Buddy®” system on QoL and symptom burden in patients undergoing initial treatment for head and neck cancer [29]. Both studies used the same group of patients. Forty-four patients used the “Health Buddy®” system and the feasibility and acceptance of the intervention were evaluated by accrual rate (56.7%), utilization (86.3%), nurse-initiated contacts (73%), and/or satisfaction [13]. The Head and Neck Cancer Therapy Assessment Scale (FACT-H & N) and the Memory Symptom Assessment Scale (MSAS) were used to evaluate the quality of life and symptom burden [13,29]. The inference of the studies cited is that TH was achievable, well-accepted, and often used by patients, although an adherence bias was identified due to the high frequency of contacts made by nurses [13]. THimproved some aspects of posttreatment QoL and symptom burden, although there was no comparison with the control group, and the majority of the

different questionnaires to measureQoL did not show significant improvement [29].

A Dutch cohort study aimed to investigate the satisfaction and quality of life of 56 head and neck cancer survivors with the use of an online self-management application (“Oncokompas”) [30]. Patients were monitored for their quality of life (QOL) and their relationship with the app (adoption, usage, and satisfaction). An adherence of 64% of users to TH was reported, added to a 75-91% of implementation grade, a mean satisfaction score of 7.3 (SD 1.5), and a positive Net Promoter Score (NPS) of 1.9. Although the study considers “Oncokompas” viable for use, the authors recognized the need for further improvements related to marketing strategy and adaptation to a custom application in order to raise the viability and marginal satisfaction rating of users.

Some authors conducted two RCTs studies in a group of 14 hospitals in the Netherlands, assessing the efficacy, reach, and usage of “Oncokompas” by evaluating health-related quality of life (HRQOL), generic and specific tumor symptoms, and personalized options of supportive care [31] and a secondary analysis on most benefited subgroups of cancer survivors with “Oncokompas” use [32]. A total of 185 HNC survivors were evaluated. The control group has received access to “Oncokompas” after six months. For HNC survivors, the course of the symptoms pain in the mouth ($p = 0.010$]), social eating ($p = 0.038$]), swallowing ($p = 0.045$]), coughing ($p = 0.017$]), and trismus ($p = 0.046$]) were statistically significant when comparing both groups [31]. Considering HRQOL, the most positively impacted patients were those with low to moderate self-efficacy ($p = 0.034$), those with high personal control ($p = 0.015$), and those with higher health literacy scores ($p = 0.035$). Besides, HNC patients with higher baseline symptoms, such as mouth pain, social eating, swallowing, cough, and trismus showed better health responses using “Oncokompas” [32], although weak adherence was observed where only 52% of cancer survivors overall used Oncokompas as intended, with an median of only 3.8 logins in six months, and a possible bias towards tumor-specific symptoms.

3.5 DISCUSSION

This systematic review evaluated the use of TH in monitoring patients with

HNC regarding the model of technology used, user adherence to technology, user satisfaction, and quality of life. Eight included studies [13, 28-34] showed that remote monitoring and/or self-management of symptoms via mobile apps were feasible for most patients, with satisfactory degrees of acceptability, satisfaction, usability, and adherence. Two included studies [31,32] showed that health-related quality of life (HRQoL) improved with the use of remote technologies for TH, associated with low to moderate self-efficacy, higher personal control, and higher knowledge of health and with clinically acceptable levels of accuracy compared to traditional clinical evaluation. In this review, the studies demonstrated the use of mobile applications [33,34], web-based programs [28,30-32], and devices connected to the line telephone [29,13] for monitoring and/or self-management of patients with HNC.

Patient adherence to the use of remote technology depends on several factors, among them, the guarantee of access, the moment when the technology starts to be used to the monitoring of cancer, and the degree of use. In the case of the web-based program “My Journey Ahead”, most participants (70%) visited the program more than once and 61% viewed all units of the program. Patients who did not log in (without adherence) reported lower levels of self-efficacy to cope with the disease at the start of the study. The patients who joined the program recommended that having access to it at the beginning of their experience with cancer would have been useful [28]. The “Health Buddy®” device had an median percentage of use of 94.2%, demonstrating that most patients systematically used the TH device and, therefore, a good rate of adherence [13].

The “Oncokompas” showed a 64% rate of adherence and a level of use between 75 and 91%, confirming that the ratio of adherence can be predicted by the way a remote technology is classified in terms of usefulness and ease of use, and the self-efficacy of participants in relation to information technology [30,35]. The use of the “mHealth” app demonstrated an increase in the three acceptance variables: intention to use (3.02), perceived utility (2.95), and perceived ease of use (3.01). This result indicates that familiarity with the “mHealth” application reduced uncertainty and increased the acceptance of its use, as well as its adherence. And the “HeNeA” application found that perceived utility was positively associated with usability ($\beta = 1$, $p = 0.01$) and that user acceptance was positively associated with both perceived utility ($\beta = 0.896$, $p = 0.006$) regarding usability ($\beta = 0.833$, $p = 0.006$), and thus, the

perceived utility and usability contributed to user acceptance, and consequently, adherence of use, with the same statistical significance [33].

Considering the proportion of adherence, one study [33] showed high adherence (91%) of patients to the technology (P = 0.91; 95% CI - [0.74 -1.08]). Five studies [13,29,31,32,24] showed between 50% to 70% adherence to the use of the TH tool and two studies [28,30] showed an average above 70% adherence to the use of the TH tool. Our findings are in accordance with the literature that demonstrates that, from the maintenance of patient's adherence to remote technologies, TH presents itself as a promising method to improve self-management and can be used as part of a comprehensive monitoring program [36-38]. Figure 2 shows the trend/proportion graph of users' adherence to the use of the TH tool with a variation from 50% to 91%.

Figure 2 should be placed here.

User satisfaction with the use of remote technologies was assessed by four studies. "Health Buddy®" users were favorable to the system in terms of ease of installation and useful content and reported an improvement in their ability to self-manage the disease and treatment'sside effects [13]. At "Oncokompas" the average satisfaction score was 7.3 (SD 1.5), considering the application friendly (76.0%, mean score 7.1, SD 1.6) [31]. In the case of "HeNeA", the overall satisfaction rate was 18.5 [33]. Likewise, when adhering to the application, the perceived usefulness and usability contributed to the user's acceptance and, thus, to the high level of satisfaction [34]. Users showed a high acceptance of the "mHealth" app, concerning the intended use, utility, and perceived ease of use. These three aspects of acceptability increased after the intervention (P < 0.01), with great significance in the satisfaction of using the application [34]. In several studies, remote technologies have demonstrated a high level of user satisfaction in monitoring health conditions, in line with the findings of this review [39,40].

The effect of remote technologies on HRQoL in patients with HNC was assessed by 6 studies. Relationships between the percentage used, Physical Well-Being, and Emotional Well- Being during treatment suggest that "Health Buddy®" use resulted in physical and emotional aspects of QOL improvements [13]. Although findings from previous studies showed a more gradual return to baseline quality of life [4], the application of "Health Buddy®" showed a faster improvement [29].

The effect of “Oncokompas” on HRQOL seems to last longer among cancer patients with low to moderate self-efficacy, survivors with greater personal control, and those with higher health literacy [32]. In the case of the “mHealth” application, there was an improvement in Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) on Head and Neck Module (EORTC QLQ-H&N35) and a reduction in care needs. There was a reduction in the baseline of the total QLQ-H&N35 scores in the experimental group (32.15) and in the control group (28.99) when compared with the values afterthree months of intervention, both in the experimental group (24.91) and in the control group (24.63) [34].

With the use of “mHealth”, although it has not shown statistically significant results, patients reported improvement in QLQ-H&N35 after the intervention [41]. The “HeneA” application showed a negative association ($\beta = -0, 0249$, $p = 0.007$) between the EuroQoL and the severity of the symptoms. The greater the severity of the reported symptoms, the lower the EuroQoL [33]. In cancer patients, remote technologies can act as an incentive and provide the tools to improve HRQOL with low to moderate self-efficacy. Cancer patients with higher personal control probably feel in control of the app, which leads to an early improvement in HRQOL. Health literacy is known to be an important factor in eHealth interventions [42] and is positively associated with HRQOL [43-45].

However, there are inherent negative aspects of using TH’s applications in the monitoring of cancer patients. SymptomCare @ Home [46,47] establishes a daily monitoring of symptoms through an interactive voice response on the phone, which can be considered uncomfortable for patients in long-term follow-up. Likewise, exclusively web-based interventions [48,49] tend to be impractical, due to the need for an internet connection when patients want to report a symptom, also having to log in every time with their username and password. In telephone-based care systems, it is necessary to improve communication methods in order to make the interaction between patient/provider more effective and improve symptom management [50-52].

This review brought forward some limitations inherent to the studies evaluated. The studies had a probable selection bias, with the use of convenience samples, some with modest number of participants or evaluators [13, 28-33]; overload of content and information for users of remote technologies [13,28,30]; use

in a single institution [29,34]; investment of time required to complete the application [30]; short follow-up period [30,34]; lack of evaluation of the improvement of the care process and availability on single mobile platform of remote technology [33] and the possibility that the results do not reflect the situation of each user [30]. Despite the limitations, our results point to the potential of using viable and acceptable remote technology tools in monitoring the HNC, requiring qualitative research with a deeper investigation based on a longitudinal analysis.

3.6 CONCLUSION

An analysis was carried out, through the systematization of evidence in the literature, of the use of TH in the monitoring of patients with head and neck cancer regarding the application used, user adherence to the technology, user satisfaction and user quality of life. Telehealth monitoring using remote technologies has proven to be an acceptable and viable means of educating and supporting patients during their HNC treatment. Although the selected TH interventions, in this review, use automated asynchronous methods, they have demonstrated some improvement in HRQoL, availability, and adherence to use. There is need for a more user-friendly interface, adequate user experience assessment, and the concrete applicability of TH technologies for monitoring patients with HNC, in order to legitimize the cost-effectiveness of developing long-term multicenter longitudinal studies term.

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Appendix 1 - Database search strategy.		
Database	Search (January the 21st, 2021)	References
PubMed	#1 - "Mouth Neoplasms"[All Fields] OR "Mouth Neoplasm"[All Fields] OR "neoplasm mouth"[All Fields] OR "neoplasms oral"[All Fields] OR "neoplasm oral"[All Fields] OR "Oral Neoplasm"[All Fields] OR "Oral Neoplasms"[All Fields] OR "neoplasms mouth"[All Fields] OR "Cancer of Mouth"[All Fields] OR "Mouth Cancers"[All Fields] OR "Oral Cancer"[All Fields] OR "cancer oral"[All Fields] OR "cancers oral"[All Fields] OR "Oral Cancers"[All Fields] OR "Cancer of the Mouth"[All Fields] OR "Mouth Cancer"[All Fields] OR "cancer mouth"[All Fields] OR "cancers mouth"[All Fields] OR "Head and Neck Neoplasms"[All Fields] OR "neoplasms head and neck"[All Fields] OR "head neck neoplasms"[All Fields] OR "Cancer of Head and Neck"[All Fields] OR "Head and Neck Cancer"[All Fields] OR "Cancer of the Head and Neck"[All Fields] OR "Upper Aerodigestive Tract Neoplasms"[All Fields] OR "UADT Neoplasms"[All Fields] OR ("Head and Neck Neoplasms"[MeSH Terms] OR ("head"[All Fields] AND "neck"[All Fields] AND "neoplasms"[All Fields]) OR "Head and Neck Neoplasms"[All Fields] OR ("neoplasm"[All Fields] AND "uadt"[All Fields])) OR "neoplasms uadt"[All Fields] OR ("Head and Neck Neoplasms"[MeSH Terms] OR ("head"[All Fields] AND "neck"[All Fields] AND "neoplasms"[All Fields]) OR "Head and Neck Neoplasms"[All Fields] OR ("uadt"[All Fields] AND "neoplasm"[All Fields])) OR ("Head and Neck Neoplasms"[MeSH Terms] OR ("head"[All Fields] AND "neck"[All Fields] AND "neoplasms"[All Fields]) OR "Head and Neck Neoplasms"[All Fields] OR ("neoplasms"[All Fields] AND "upper"[All Fields] AND "aerodigestive"[All Fields] AND "tract"[All Fields])) OR "Head Neoplasms"[All Fields] OR "neoplasms head"[All Fields] OR "Neck Neoplasms"[All Fields] OR "neoplasms neck"[All Fields] OR "Cancer of Head"[All Fields] OR "Head Cancer"[All Fields] OR "Cancer of the Head"[All Fields] OR "Cancer of Neck"[All Fields] OR "Neck Cancer"[All Fields] OR "Cancer of the Neck"[All Fields] OR "malignant disorders"[All Fields] OR ("precancerous conditions"[MeSH Terms] OR ("precancerous"[All Fields] AND "conditions"[All Fields]) OR "precancerous conditions"[All Fields] OR "premalignant"[All Fields] OR "premalign"[All Fields] OR "premalignancies"[All Fields] OR "premalignancy"[All Fields]) #2 - ("Teledentistry"[All Fields] OR "Tele-dentistry"[All Fields] OR "tele-triage"[All Fields] OR ("telemedicine"[MeSH Terms] OR "telemedicine"[All Fields] OR "telemedicine s"[All Fields]) OR "Mobile Health"[All Fields] OR "health mobile"[All Fields] OR "Mhealth"[All Fields] OR ("telehealth s"[All Fields] OR "telemedicine"[MeSH Terms] OR "telemedicine"[All Fields] OR "telehealth"[All Fields]) OR ("telemedicine"[MeSH Terms] OR "telemedicine"[All Fields] OR "ehealth"[All Fields]) OR ("telemonitor"[All Fields] OR "telemonitored"[All Fields] OR "telemonitoring"[All Fields] OR "telemonitors"[All Fields]) OR ("telementor"[All Fields] OR "telementored"[All Fields] OR "telementoring"[All Fields]) OR "Telecare"[All Fields] OR "Teleassistance"[All Fields]) OR ("asynchronous service models"[All Fields] OR "remote technologies"[All Fields] OR ("remote"[All Fields] OR "remotely"[All Fields] OR "remoteness"[All Fields] OR "remotes"[All Fields]) OR "virtual platform"[All Fields] OR "virtual platforms"[All Fields] OR "Mobile-phone-based screening"[All Fields] OR "Mobile Applications"[All Fields] OR "application mobile"[All Fields] OR "applications mobile"[All Fields] OR "Mobile Application"[All Fields] OR "Mobile Apps"[All Fields] OR "app mobile"[All Fields] OR "apps mobile"[All Fields] OR "Mobile App"[All Fields] OR "Portable Electronic Apps"[All Fields] OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("app"[All Fields] AND "portable"[All Fields] AND "electronic"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("apps"[All Fields] AND "portable"[All Fields] AND "electronic"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("electronic"[All Fields] AND "app"[All Fields] AND "portable"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("electronic"[All Fields] AND "apps"[All Fields] AND "portable"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("portable"[All Fields] AND "electronic"[All Fields] AND "app"[All Fields])) OR "Portable Electronic Applications"[All Fields] OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("application"[All Fields] AND "portable"[All Fields]	65 *(continued)*

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Appendix 1 - Database search strategy.		
Database	Search (January the 21st, 2021)	References
	AND "electronic"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("applications"[All Fields] AND "portable"[All Fields] AND "electronic"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("electronic"[All Fields] AND "application"[All Fields] AND "portable"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("electronic"[All Fields] AND "applications"[All Fields] AND "portable"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("portable"[All Fields] AND "electronic"[All Fields] AND "application"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("portable"[All Fields] AND "software"[All Fields] AND "apps"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("app"[All Fields] AND "portable"[All Fields] AND "software"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("apps"[All Fields] AND "portable"[All Fields] AND "software"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("portable"[All Fields] AND "software"[All Fields] AND "app"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("software"[All Fields] AND "app"[All Fields] AND "portable"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("software"[All Fields] AND "apps"[All Fields] AND "portable"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("portable"[All Fields] AND "software"[All Fields] AND "applications"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("application"[All Fields] AND "portable"[All Fields] AND "software"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("applications"[All Fields] AND "portable"[All Fields] AND "software"[All Fields])) OR "Portable Software Application"[All Fields] OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("software"[All Fields] AND "application"[All Fields] AND "portable"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("software"[All Fields] AND "applications"[All Fields] AND "portable"[All Fields])) OR "Computer Software"[All Fields] OR "software computer"[All Fields] OR "Computer Programs"[All Fields] OR "Computer Program"[All Fields] OR "program computer"[All Fields] OR "programs computer"[All Fields] OR "Software Tools"[All Fields] OR "Software Tool"[All Fields] OR "tool software"[All Fields] OR "tools software"[All Fields] OR "Computer Applications Software"[All Fields] OR ("software"[MeSH Terms] OR "software"[All Fields] OR ("applications"[All Fields] AND "software"[All Fields] AND "computer"[All Fields])) OR ("software"[MeSH Terms] OR "software"[All Fields] OR ("applications"[All Fields] AND "softwares"[All Fields] AND "computer"[All Fields])) OR ("software"[MeSH Terms] OR "software"[All Fields] OR ("computer"[All Fields] AND "applications"[All Fields] AND "softwares"[All Fields])) OR ("software"[MeSH Terms] OR "software"[All Fields] OR ("software"[All Fields] AND "computer"[All Fields] AND "applications"[All Fields])) OR ("software"[MeSH Terms] OR "software"[All Fields] OR ("softwares"[All Fields] AND "computer"[All Fields] AND "applications"[All Fields])) OR "Computer Software Applications"[All Fields] OR ("software"[MeSH Terms] OR "software"[All Fields] OR ("application"[All Fields] AND "computer"[All Fields] AND "software"[All Fields])) OR "applications computer software"[All Fields] OR "Computer Software Application"[All Fields] OR "software application computer"[All Fields] OR "software applications computer"[All Fields] OR "Computer Programs and Programming"[All Fields] OR "Software Engineering"[All	*(continued)*

Appendix 1 - Database search strategy.		
Database	Search (January the 21st, 2021)	References
	Fields] OR "engineering software"[All Fields] OR "virtual consultation"[All Fields] OR "virtual consultations"[All Fields] OR (("virtual"[All Fields] OR "virtuality"[All Fields] OR "virtualization"[All Fields] OR "virtualized"[All Fields] OR "virtualizing"[All Fields] OR "virtuals"[All Fields]) AND "online"[All Fields] AND ("consultancies"[All Fields] OR "consultancy"[All Fields] OR "consultant s"[All Fields] OR "consultants"[MeSH Terms] OR "consultants"[All Fields] OR "consultant"[All Fields] OR "consultative"[All Fields] OR "consulter"[All Fields] OR "consulters"[All Fields] OR "referral and consultation"[MeSH Terms] OR ("referral"[All Fields] AND "consultation"[All Fields]) OR "referral and consultation"[All Fields] OR "consult"[All Fields] OR "consultation"[All Fields] OR "consultations"[All Fields] OR "consulted"[All Fields] OR "consulting"[All Fields] OR "consults"[All Fields])) OR (("virtual"[All Fields] OR "virtuality"[All Fields] OR "virtualization"[All Fields] OR "virtualized"[All Fields] OR "virtualizing"[All Fields] OR "virtuals"[All Fields]) AND "online"[All Fields] AND ("consultancies"[All Fields] OR "consultancy"[All Fields] OR "consultant s"[All Fields] OR "consultants"[MeSH Terms] OR "consultants"[All Fields] OR "consultant"[All Fields] OR "consultative"[All Fields] OR "consulter"[All Fields] OR "consulters"[All Fields] OR "referral and consultation"[MeSH Terms] OR ("referral"[All Fields] AND "consultation"[All Fields]) OR "referral and consultation"[All Fields] OR "consult"[All Fields] OR "consultation"[All Fields] OR "consultations"[All Fields] OR "consulted"[All Fields] OR "consulting"[All Fields] OR "consults"[All Fields])) OR "Virtual Care"[All Fields] OR "E-consultation"[All Fields] OR "e-referral"[All Fields] OR "remote consultation"[All Fields] OR "tele-consultation"[All Fields] OR "video-consultation"[All Fields]) #3 - "supportive oncology"[All Fields] OR "supportive treatment"[All Fields] OR "supportive care"[All Fields] OR "Supportive therapy"[All Fields] OR "Palliative Care"[All Fields] OR "care palliative"[All Fields] OR "Palliative Treatment"[All Fields] OR "Palliative Treatments"[All Fields] OR "treatment palliative"[All Fields] OR "treatments palliative"[All Fields] OR "therapy palliative"[All Fields] OR "Palliative Therapy"[All Fields] OR "Palliative Supportive Care"[All Fields] OR "supportive care palliative"[All Fields] #4 - #1 AND #2 AND #3	
Cochrane Library	#1 - ("Mouth Neoplasms" OR "Mouth Neoplasm" OR "Neoplasm, Mouth" OR "Neoplasms, Oral" OR "Neoplasm, Oral" OR "Oral Neoplasm" OR "Oral Neoplasms" OR "Neoplasms, Mouth" OR "Cancer of Mouth" OR "Mouth Cancers" OR "Oral Cancer" OR "Cancer, Oral" OR "Cancers, Oral" OR "Oral Cancers" OR "Cancer of the Mouth" OR "Mouth Cancer" OR "Cancer, Mouth" OR "Cancers, Mouth" OR "Head and Neck Neoplasms" OR "Neoplasms, Head and Neck" OR "Head, Neck Neoplasms" OR "Cancer of Head and Neck" OR "Head and Neck Cancer" OR "Cancer of the Head and Neck" OR "Upper Aerodigestive Tract Neoplasms" OR "UADT Neoplasms" OR "Neoplasm, UADT" OR "Neoplasms, UADT" OR "UADT Neoplasm" OR "Neoplasms, Upper Aerodigestive Tract" OR "Head Neoplasms" OR "Neoplasms, Head" OR "Neck Neoplasms" OR "Neoplasms, Neck" OR "Cancer of Head" OR "Head Cancer" OR "Cancer of the Head" OR "Cancer of Neck" OR "Neck Cancer" OR "Cancer of the Neck" OR "malignant disorders" OR premalignant) #2 - (Teledentistry OR Tele-dentistry OR tele-triage OR Telemedicine OR "Mobile Health" OR "Health, Mobile" OR "Mhealth" OR Telehealth OR Ehealth OR Telemonitoring OR Telementoring OR Telecare OR Teleassistance) OR ("asynchronous service models" OR "remote technologies" OR "remote techynology" OR "virtual platform" OR "virtual platforms" OR "Mobile-phone-based screening" OR "Mobile Applications" OR "Application, Mobile" OR "Applications, Mobile" OR "Mobile Application" OR "Mobile Apps" OR "App, Mobile" OR "Apps, Mobile" OR "Mobile App" OR "Portable Electronic Apps" OR "App, Portable Electronic" OR "Apps, Portable Electronic" OR "Electronic App, Portable" OR "Electronic Apps, Portable" OR "Portable Electronic App" OR "Portable Electronic Applications" OR "Application, Portable Electronic" OR "Applications, Portable Electronic" OR "Electronic Application, Portable" OR "Electronic Applications, Portable" OR "Portable Electronic Application" OR "Portable Software Apps" OR "App, Portable Software" OR "Apps, Portable Software" OR "Portable Software App" OR "Software App, Portable" OR "Software Apps, Portable" OR "Portable	21 *(continued)*

Appendix 1 - Database search strategy.		
Database	Search (January the 21st, 2021)	References
	Software Applications" OR "Application, Portable Software" OR "Applications, Portable Software" OR "Portable Software Application" OR "Software Application, Portable" OR "Software Applications, Portable" OR "Computer Software" OR "Software, Computer" OR "Computer Programs" OR "Computer Program" OR "Program, Computer" OR "Programs, Computer" OR "Software Tools" OR "Software Tool" OR "Tool, Software" OR "Tools, Software" OR "Computer Applications Software" OR "Applications Software, Computer" OR "Applications Softwares, Computer" OR "Computer Applications Softwares" OR "Software, Computer Applications" OR "Softwares, Computer Applications" OR "Computer Software Applications" OR "Application, Computer Software" OR "Applications, Computer Software" OR "Computer Software Application" OR "Software Application, Computer" OR "Software Applications, Computer" OR "Computer Programs and Programming" OR "Software Engineering" OR "Engineering, Software" OR "virtual consultation" OR "virtual consultations" OR "Virtual online consultation" OR "Virtual online consultations" OR "Virtual Care" OR "E-consultation" OR "e-referral" OR "remote consultation" OR tele-consultation OR "video-consultation") #3 - ("supportive oncology" OR "supportive treatment" OR "supportive care" OR "Supportive therapy" OR "Palliative Care" OR "Care, Palliative" OR "Palliative Treatment" OR "Palliative Treatments" OR "Treatment, Palliative" OR "Treatments, Palliative" OR "Therapy, Palliative" OR "Palliative Therapy" OR "Palliative Supportive Care" OR "Supportive Care, Palliative") #4 - #1 AND #2 AND #3	
Scopus	(TITLE-ABS-KEY (("Mouth Neoplasms" OR "Mouth Neoplasm" OR "Neoplasm, Mouth" OR "Neoplasms, Oral" OR "Neoplasm, Oral" OR "Oral Neoplasm" OR "Oral Neoplasms" OR "Neoplasms, Mouth" OR "Cancer of Mouth" OR "Mouth Cancers" OR "Oral Cancer" OR "Cancer, Oral" OR "Cancers, Oral" OR "Oral Cancers" OR "Cancer of the Mouth" OR "Mouth Cancer" OR "Cancer, Mouth" OR "Cancers, Mouth" OR "Head and Neck Neoplasms" OR "Neoplasms, Head and Neck" OR "Head, Neck Neoplasms" OR "Cancer of Head and Neck" OR "Head and Neck Cancer" OR "Cancer of the Head and Neck" OR "Upper Aerodigestive Tract Neoplasms" OR "UADT Neoplasms" OR "Neoplasm, UADT" OR "Neoplasms, UADT" OR "UADT Neoplasm" OR "Neoplasms, Upper Aerodigestive Tract" OR "Head Neoplasms" OR "Neoplasms, Head" OR "Neck Neoplasms" OR "Neoplasms, Neck" OR "Cancer of Head" OR "Head Cancer" OR "Cancer of the Head" OR "Cancer of Neck" OR "Neck Cancer" OR "Cancer of the Neck" OR "malignant disorders" OR premalignant)) AND TITLE-ABS-KEY ((teledentistry OR tele-dentistry OR tele-triage OR telemedicine OR "Mobile Health" OR "Health, Mobile" OR "Mhealth" OR telehealth OR ehealth OR telemonitoring OR telementoring OR telecare OR teleassistance) OR ("asynchronous service models" OR "remote technologies" OR "remote techynology" OR "virtual platform" OR "virtual platforms" OR "Mobile-phone-based screening" OR "Mobile Applications" OR "Application, Mobile" OR "Applications, Mobile" OR "Mobile Application" OR "Mobile Apps" OR "App, Mobile" OR "Apps, Mobile" OR "Mobile App" OR "Portable Electronic Apps" OR "App, Portable Electronic" OR "Apps, Portable Electronic" OR "Electronic App, Portable" OR "Electronic Apps, Portable" OR "Portable Electronic App" OR "Portable Electronic Applications" OR "Application, Portable Electronic" OR "Applications, Portable Electronic" OR "Electronic Application, Portable" OR "Electronic Applications, Portable" OR "Portable Electronic Application" OR "Portable Software Apps" OR "App, Portable Software" OR "Apps, Portable Software" OR "Portable Software App" OR "Software App, Portable" OR "Software Apps, Portable" OR "Portable Software Applications" OR "Application, Portable Software" OR "Applications, Portable Software" OR "Portable Software Application" OR "Software Application, Portable" OR "Software Applications, Portable" OR "Computer Software" OR "Software, Computer" OR "Computer Programs" OR "Computer Program" OR "Program, Computer" OR "Programs, Computer" OR "Software Tools" OR "Software Tool" OR "Tool, Software" OR "Tools, Software" OR "Computer Applications	24

(continued)

Appendix 1 - Database search strategy.		
Database	Search (January the 21st, 2021)	References
	Software" OR "Applications Software, Computer" OR "Applications Softwares, Computer" OR "Computer Applications Softwares" OR "Software, Computer Applications" OR "Softwares, Computer Applications" OR "Computer Software Applications" OR "Application, Computer Software" OR "Applications, Computer Software" OR "Computer Software Application" OR "Software Application, Computer" OR "Software Applications, Computer" OR "Computer Programs and Programming" OR "Software Engineering" OR "Engineering, Software" OR "virtual consultation" OR "virtual consultations" OR "Virtual online consultation" OR "Virtual online consultations" OR "Virtual Care" OR "E-consultation" OR "e-referral" OR "remote consultation" OR tele-consultation OR "video-consultation")) AND TITLE-ABS-KEY (("supportive oncology" OR "supportive treatment" OR "supportive care" OR "Supportive therapy" OR "Palliative Care" OR "Care, Palliative" OR "Palliative Treatment" OR "Palliative Treatments" OR "Treatment, Palliative" OR "Treatments, Palliative" OR "Therapy, Palliative" OR "Palliative Therapy" OR "Palliative Supportive Care" OR "Supportive Care, Palliative"))) View less	
Web of Science	#1- TS=("Mouth Neoplasms" OR "Mouth Neoplasm" OR "Neoplasm, Mouth" OR "Neoplasms, Oral" OR "Neoplasm, Oral" OR "Oral Neoplasm" OR "Oral Neoplasms" OR "Neoplasms, Mouth" OR "Cancer of Mouth" OR "Mouth Cancers" OR "Oral Cancer" OR "Cancer, Oral" OR "Cancers, Oral" OR "Oral Cancers" OR "Cancer of the Mouth" OR "Mouth Cancer" OR "Cancer, Mouth" OR "Cancers, Mouth" OR "Head and Neck Neoplasms" OR "Neoplasms, Head and Neck" OR "Head, Neck Neoplasms" OR "Cancer of Head and Neck" OR "Head and Neck Cancer" OR "Cancer of the Head and Neck" OR "Upper Aerodigestive Tract Neoplasms" OR "UADT Neoplasms" OR "Neoplasm, UADT" OR "Neoplasms, UADT" OR "UADT Neoplasm" OR "Neoplasms, Upper Aerodigestive Tract" OR "Head Neoplasms" OR "Neoplasms, Head" OR "Neck Neoplasms" OR "Neoplasms, Neck" OR "Cancer of Head" OR "Head Cancer" OR "Cancer of the Head" OR "Cancer of Neck" OR "Neck Cancer" OR "Cancer of the Neck" OR "malignant disorders" OR premalignant) Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=Todos os anos #2-TS=(Teledentistry OR Tele-dentistry OR tele-triage OR Telemedicine OR "Mobile Health" OR "Health, Mobile" OR "Mhealth" OR Telehealth OR Ehealth OR Telemonitoring OR Telementoring OR Telecare OR Teleassistance OR "asynchronous service models" OR "remote technologies" OR "remote techynology" OR "virtual platform" OR "virtual platforms" OR "Mobile-phone-based screening" OR "Mobile Applications" OR "Application, Mobile" OR "Applications, Mobile" OR "Mobile Application" OR "Mobile Apps" OR "App, Mobile" OR "Apps, Mobile" OR "Mobile App" OR "Portable Electronic Apps" OR "App, Portable Electronic" OR "Apps, Portable Electronic" OR "Electronic App, Portable" OR "Electronic Apps, Portable" OR "Portable Electronic App" OR "Portable Electronic Applications" OR "Application, Portable Electronic" OR "Applications, Portable Electronic" OR "Electronic Application, Portable" OR "Electronic Applications, Portable" OR "Portable Electronic Application" OR "Portable Software Apps" OR "App, Portable Software" OR "Apps, Portable Software" OR "Portable Software App" OR "Software App, Portable" OR "Software Apps, Portable" OR "Portable Software Applications" OR "Application, Portable Software" OR "Applications, Portable Software" OR "Portable Software Application" OR "Software Application, Portable" OR "Software Applications, Portable" OR "Computer Software" OR "Software, Computer" OR "Computer Programs" OR "Computer Program" OR "Program, Computer" OR "Programs, Computer" OR "Software Tools" OR "Software Tool" OR "Tool, Software" OR "Tools, Software" OR "Computer Applications Software" OR "Applications Software, Computer" OR "Applications Softwares, Computer" OR "Computer Applications Softwares" OR "Software, Computer Applications" OR "Softwares, Computer Applications" OR "Computer Software Applications" OR "Application, Computer Software" OR "Applications, Computer Software" OR "Computer Software Application" OR "Software Application, Computer" OR "Software Applications, Computer" OR "Computer Programs and Programming" OR "Software Engineering" OR "Engineering, Software" OR "virtual consultation" OR "virtual consultations" OR "Virtual online consultation" OR "Virtual online consultations" OR "Virtual Car	19 *(continued)*

Appendix 1 - Database search strategy.		
Database	Search (January the 21st, 2021)	References
	e" OR "E-consultation" OR "e-referral" OR "remote consultation" OR tele-consultation OR "video-consultation") Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=Todos os anos #3– TS=("supportive oncology" OR "supportive treatment" OR "supportive care" OR "Supportive therapy" OR "Palliative Care" OR "Care, Palliative" OR "Palliative Treatment" OR "Palliative Treatments" OR "Treatment, Palliative" OR "Treatments, Palliative" OR "Therapy, Palliative" OR "Palliative Therapy" OR "Palliative Supportive Care" OR "Supportive Care, Palliative") #4 - #3 AND #2 AND #1 Índices=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Tempo estipulado=Todos os anos	
Lilacs (via VHL Regional Portal)	(("Mouth Neoplasms" OR "Mouth Neoplasm" OR "Neoplasm, Mouth" OR "Neoplasms, Oral" OR "Neoplasm, Oral" OR "Oral Neoplasm" OR "Oral Neoplasms" OR "Neoplasms, Mouth" OR "Cancer of Mouth" OR "Mouth Cancers" OR "Oral Cancer" OR "Cancer, Oral" OR "Cancers, Oral" OR "Oral Cancers" OR "Cancer of the Mouth" OR "Mouth Cancer" OR "Cancer, Mouth" OR "Cancers, Mouth" OR "Head and Neck Neoplasms" OR "Neoplasms, Head and Neck" OR "Head, Neck Neoplasms" OR "Cancer of Head and Neck" OR "Head and Neck Cancer" OR "Cancer of the Head and Neck" OR "Upper Aerodigestive Tract Neoplasms" OR "UADT Neoplasms" OR "Neoplasm, UADT" OR "Neoplasms, UADT" OR "UADT Neoplasm" OR "Neoplasms, Upper Aerodigestive Tract" OR "Head Neoplasms" OR "Neoplasms, Head" OR "Neck Neoplasms" OR "Neoplasms, Neck" OR "Cancer of Head" OR "Head Cancer" OR "Cancer of the Head" OR "Cancer of Neck" OR "Neck Cancer" OR "Cancer of the Neck" OR "malignant disorders" OR premalignant)) AND ((Teledentistry OR Tele-dentistry OR tele-triage OR Telemedicine OR "Mobile Health" OR "Health, Mobile" OR "Mhealth" OR Telehealth OR Ehealth OR Telemonitoring OR Telementoring OR Telecare OR Teleassistance) OR ("asynchronous service models" OR "remote technologies" OR "remote techynology" OR "virtual platform" OR "virtual platforms" OR "Mobile-phone-based screening" OR "Mobile Applications" OR "Application, Mobile" OR "Applications, Mobile" OR "Mobile Application" OR "Mobile Apps" OR "App, Mobile" OR "Apps, Mobile" OR "Mobile App" OR "Portable Electronic Apps" OR "App, Portable Electronic" OR "Apps, Portable Electronic" OR "Electronic App, Portable" OR "Electronic Apps, Portable" OR "Portable Electronic App" OR "Portable Electronic Applications" OR "Application, Portable Electronic" OR "Applications, Portable Electronic" OR "Electronic Application, Portable" OR "Electronic Applications, Portable" OR "Portable Electronic Application" OR "Portable Software Apps" OR "App, Portable Software" OR "Apps, Portable Software" OR "Portable Software App" OR "Software App, Portable" OR "Software Apps, Portable" OR "Portable Software Applications" OR "Application, Portable Software" OR "Applications, Portable Software" OR "Portable Software Application" OR "Software Application, Portable" OR "Software Applications, Portable" OR "Computer Software" OR "Software, Computer" OR "Computer Programs" OR "Computer Program" OR "Program, Computer" OR "Programs, Computer" OR "Software Tools" OR "Software Tool" OR "Tool, Software" OR "Tools, Software" OR "Computer Applications Software" OR "Applications Software, Computer" OR "Applications Softwares, Computer" OR "Computer Applications Softwares" OR "Software, Computer Applications" OR "Softwares, Computer Applications" OR "Computer Software Applications" OR "Application, Computer Software" OR "Applications, Computer Software" OR "Computer Software Application" OR "Software Application, Computer" OR "Software Applications, Computer" OR "Computer Programs and Programming" OR "Software Engineering" OR "Engineering, Software" OR "virtual consultation" OR "virtual consultations" OR "Virtual online consultation" OR "Virtual online consultations" OR "Virtual Care" OR "E-consultation" OR "e-referral" OR "remote consultation" OR tele-consultation OR "video-consultation")) AND (("supportive oncology" OR "supportive treatment" OR "supportive care" OR "Supportive therapy" OR "Palliative Care" OR "Care, Palliative" OR "Palliative Treatment" OR "Palliative Treatments" OR "Treatment, Palliative" OR "Treatments, Palliative" OR "Therapy, Palliative" OR "Palliative Therapy" OR "Palliative Supportive Care" OR "Supportive Care, Palliative"))	1

(continued)

Appendix 1 - Database search strategy.		
Database	Search (January the 21st, 2021)	References
EMBASE	((((((('mouth neoplasms':ti,ab,kw OR 'mouth neoplasm':ti,ab,kw OR 'neoplasm, mouth':ti,ab,kw OR 'neoplasms, oral':ti,ab,kw OR 'neoplasm, oral':ti,ab,kw OR 'oral neoplasm':ti,ab,kw OR 'oral neoplasms':ti,ab,kw OR 'neoplasms, mouth':ti,ab,kw OR 'cancer of mouth':ti,ab,kw OR 'mouth cancers':ti,ab,kw OR 'oral cancer':ti,ab,kw OR 'cancer, oral':ti,ab,kw OR 'cancers, oral':ti,ab,kw OR 'oral cancers':ti,ab,kw OR 'cancer of the mouth':ti,ab,kw OR 'mouth cancer':ti,ab,kw OR 'cancer, mouth':ti,ab,kw OR 'cancers, mouth':ti,ab,kw OR head:ti,ab,kw) AND 'neck neoplasms':ti,ab,kw OR 'neoplasms, head':ti,ab,kw) AND neck:ti,ab,kw OR 'head, neck neoplasms':ti,ab,kw OR 'cancer of head':ti,ab,kw) AND neck:ti,ab,kw OR head:ti,ab,kw) AND 'neck cancer':ti,ab,kw OR 'cancer of the head':ti,ab,kw) AND neck:ti,ab,kw OR 'upper aerodigestive tract neoplasms':ti,ab,kw OR 'uadt neoplasms':ti,ab,kw OR 'neoplasm, uadt':ti,ab,kw OR 'neoplasms, uadt':ti,ab,kw OR 'uadt neoplasm':ti,ab,kw OR 'neoplasms, upper aerodigestive tract':ti,ab,kw OR 'head neoplasms':ti,ab,kw OR 'neoplasms, head':ti,ab,kw OR 'neck neoplasms':ti,ab,kw OR 'neoplasms, neck':ti,ab,kw OR 'cancer of head':ti,ab,kw OR 'head cancer':ti,ab,kw OR 'cancer of the head':ti,ab,kw OR 'cancer of neck':ti,ab,kw OR 'neck cancer':ti,ab,kw OR 'cancer of the neck':ti,ab,kw OR 'malignant disorders':ti,ab,kw OR premalignant:ti,ab,kw) AND (teledentistry OR 'tele dentistry' OR 'tele triage' OR telemedicine OR 'mobile health' OR 'health, mobile' OR 'mhealth' OR telehealth OR ehealth OR telemonitoring OR telementoring OR telecare OR teleassistance OR (('asynchronous service models':ti,ab,kw OR 'remote technologies':ti,ab,kw OR 'remote techynology':ti,ab,kw OR 'virtual platform':ti,ab,kw OR 'virtual platforms':ti,ab,kw OR 'mobile-phone-based screening':ti,ab,kw OR 'mobile applications':ti,ab,kw OR 'application, mobile':ti,ab,kw OR 'applications, mobile':ti,ab,kw OR 'mobile application':ti,ab,kw OR 'mobile apps':ti,ab,kw OR 'app, mobile':ti,ab,kw OR 'apps, mobile':ti,ab,kw OR 'mobile app':ti,ab,kw OR 'portable electronic apps':ti,ab,kw OR 'app, portable electronic':ti,ab,kw OR 'apps, portable electronic':ti,ab,kw OR 'electronic app, portable':ti,ab,kw OR 'electronic apps, portable':ti,ab,kw OR 'portable electronic app':ti,ab,kw OR 'portable electronic applications':ti,ab,kw OR 'application, portable electronic':ti,ab,kw OR 'applications, portable electronic':ti,ab,kw OR 'electronic application, portable':ti,ab,kw OR 'electronic applications, portable':ti,ab,kw OR 'portable electronic application':ti,ab,kw OR 'portable software apps':ti,ab,kw OR 'app, portable software':ti,ab,kw OR 'apps, portable software':ti,ab,kw OR 'portable software app':ti,ab,kw OR 'software app, portable':ti,ab,kw OR 'software apps, portable':ti,ab,kw OR 'portable software applications':ti,ab,kw OR 'application, portable software':ti,ab,kw OR 'applications, portable software':ti,ab,kw OR 'portable software application':ti,ab,kw OR 'software application, portable':ti,ab,kw OR 'software applications, portable':ti,ab,kw OR 'computer software':ti,ab,kw OR 'software, computer':ti,ab,kw OR 'computer program':ti,ab,kw OR 'program, computer':ti,ab,kw OR 'programs, computer':ti,ab,kw OR 'software tools':ti,ab,kw OR 'software tool':ti,ab,kw OR 'tool, software':ti,ab,kw OR 'tools, software':ti,ab,kw OR 'computer applications software':ti,ab,kw OR 'applications software, computer':ti,ab,kw OR 'applications softwares, computer':ti,ab,kw OR 'computer applications softwares':ti,ab,kw OR 'software, computer applications':ti,ab,kw OR 'softwares, computer applications':ti,ab,kw OR 'computer software applications':ti,ab,kw OR 'application, computer software':ti,ab,kw OR 'applications, computer software':ti,ab,kw OR 'computer software application':ti,ab,kw OR 'software application, computer':ti,ab,kw OR 'software applications, computer':ti,ab,kw OR 'computer programs':ti,ab,kw) AND programming:ti,ab,kw) OR 'software engineering':ti,ab,kw OR 'engineering, software':ti,ab,kw OR 'virtual consultation':ti,ab,kw OR 'virtual consultations':ti,ab,kw OR 'virtual online consultation':ti,ab,kw OR 'virtual online consultations':ti,ab,kw OR 'virtual care':ti,ab,kw OR 'e-consultation':ti,ab,kw OR 'e-referral':ti,ab,kw OR 'remote consultation':ti,ab,kw OR 'tele consultation':ti,ab,kw OR 'video-consultation':ti,ab,kw) AND ('supportive oncology':ti,ab,kw OR 'supportive treatment':ti,ab,kw OR 'supportive care':ti,ab,kw OR 'supportive therapy':ti,ab,kw OR 'palliative care':ti,ab,kw OR 'care, palliative':ti,ab,kw OR 'palliative treatment':ti,ab,kw OR 'palliative treatments':ti,ab,kw OR 'treatment, palliative':ti,ab,kw OR 'treatments, palliative':ti,ab,kw OR 'therapy, palliative':ti,ab,kw OR 'palliative therapy':ti,ab,kw OR 'palliative supportive care':ti,ab,kw OR 'supportive care, palliative':ti,ab,kw)	23

(continued)

Appendix 1 - Database search strategy.		
Database	Search (January the 21st, 2021)	References
Open Grey	("Mouth Neoplasms" OR "Mouth Neoplasm" OR "Neoplasm, Mouth" OR "Neoplasms, Oral" OR "Neoplasm, Oral" OR "Oral Neoplasm" OR "Oral Neoplasms" OR "Neoplasms, Mouth" OR "Cancer of Mouth" OR "Mouth Cancers" OR "Oral Cancer" OR "Cancer, Oral" OR "Cancers, Oral" OR "Oral Cancers" OR "Cancer of the Mouth" OR "Mouth Cancer" OR "Cancer, Mouth" OR "Cancers, Mouth" OR "Head and Neck Neoplasms" OR "Neoplasms, Head and Neck" OR "Head, Neck Neoplasms" OR "Cancer of Head and Neck" OR "Head and Neck Cancer" OR "Cancer of the Head and Neck" OR "Upper Aerodigestive Tract Neoplasms" OR "UADT Neoplasms" OR "Neoplasm, UADT" OR "Neoplasms, UADT" OR "UADT Neoplasm" OR "Neoplasms, Upper Aerodigestive Tract" OR "Head Neoplasms" OR "Neoplasms, Head" OR "Neck Neoplasms" OR "Neoplasms, Neck" OR "Cancer of Head" OR "Head Cancer" OR "Cancer of the Head" OR "Cancer of Neck" OR "Neck Cancer" OR "Cancer of the Neck" OR "malignant disorders" OR premalignant) AND (Teledentistry OR Tele-dentistry OR tele-triage OR Telemedicine OR "Mobile Health" OR "Health, Mobile" OR "Mhealth" OR Telehealth OR Ehealth OR Telemonitoring OR Telementoring OR Telecare OR Teleassistance) OR ("asynchronous service models" OR "remote technologies" OR "remote techynology" OR "virtual platform" OR "virtual platforms" OR "Mobile-phone-based screening" OR "Mobile Applications" OR "Application, Mobile" OR "Applications, Mobile" OR "Mobile Application" OR "Mobile Apps" OR "App, Mobile" OR "Apps, Mobile" OR "Mobile App" OR "Portable Electronic Apps" OR "App, Portable Electronic" OR "Apps, Portable Electronic" OR "Electronic App, Portable" OR "Electronic Apps, Portable" OR "Portable Electronic App" OR "Portable Electronic Applications" OR "Application, Portable Electronic" OR "Applications, Portable Electronic" OR "Electronic Application, Portable" OR "Electronic Applications, Portable" OR "Portable Electronic Application" OR "Portable Software Apps" OR "App, Portable Software" OR "Apps, Portable Software" OR "Portable Software App" OR "Software App, Portable" OR "Software Apps, Portable" OR "Portable Software Applications" OR "Application, Portable Software" OR "Applications, Portable Software" OR "Portable Software Application" OR "Software Application, Portable" OR "Software Applications, Portable" OR "Computer Software" OR "Software, Computer" OR "Computer Programs" OR "Computer Program" OR "Program, Computer" OR "Programs, Computer" OR "Software Tools" OR "Software Tool" OR "Tool, Software" OR "Tools, Software" OR "Computer Applications Software" OR "Applications Software, Computer" OR "Applications Softwares, Computer" OR "Computer Applications Softwares" OR "Software, Computer Applications" OR "Softwares, Computer Applications" OR "Computer Software Applications" OR "Application, Computer Software" OR "Applications, Computer Software" OR "Computer Software Application" OR "Software Application, Computer" OR "Software Applications, Computer" OR "Computer Programs and Programming" OR "Software Engineering" OR "Engineering, Software" OR "virtual consultation" OR "virtual consultations" OR "Virtual online consultation" OR "Virtual online consultations" OR "Virtual Care" OR "E-consultation" OR "e-referral" OR "remote consultation" OR tele-consultation OR "video-consultation") AND ("supportive oncology" OR "supportive treatment" OR "supportive care" OR "Supportive therapy" OR "Palliative Care" OR "Care, Palliative" OR "Palliative Treatment" OR "Palliative Treatments" OR "Treatment, Palliative" OR "Treatments, Palliative" OR "Therapy, Palliative" OR "Palliative Therapy" OR "Palliative Supportive Care" OR "Supportive Care, Palliative")	0
Google Scholar	With all words ("Oral Cancer" OR "Head and Neck Neoplasms" OR "Cancer of the Head and Neck" OR "malignant disorders") AND (Teledentistry OR Telemedicine OR Telehealth) AND ("supportive oncology" OR "supportive treatment" OR "Palliative Care" OR "Palliative Treatment")	240
JSTOR	((("Oral Cancer" OR "Head and Neck Neoplasms" OR "Cancer of the Head and Neck") AND (Teledentistry OR Telemedicine OR Telehealth)) AND ("supportive oncology" OR "supportive treatment"))	0

(continued)

Appendix 2 - Excluded articles and reasons for exclusion (n=11).

Author, year	Reasons for exclusions
Ferrua M. (1), 2019	03
Head BA. (2), 2009	07
Keeney C. (3), 2010	03
Li Y. (4), 2018	08
Lin HY. (5), 2015	14
Matthijs de Wit L. (6), 2019	10
Ratnasekera N. (7), 2020	02
Russell L. (8), 2019	11
Van Der Hout A. (9), 2019	03
Van Der Hout, A. (10), 2019	03
Wang HL. (11), 2019	14

1 - literature reviews and Systematic reviews;; 2 – Editorials/Letters, case reports and series cases; 3 - Conferences, Summaries, abstracts and posters; 4 - In vitro studies; 5 - Studies of animal models; 6 - Thesis and Dissertations and book chapters; 7 - Pipelines, guidelines and research protocols; 8 - Qualitative studies; 9 - Studies that do not use remote technologies; 10 - Studies evaluating other medical/dental specialties, hospitals or clinics; 11 - Studies telemonitoring other types of cancer; 12 - Telemonitoring's studies of other comorbidities (cardiovascular, conditions, heart failure, Chronic Obstructive Pulmonary Disease, HIV/AIDS, obstetric disease, Asthma, hypertension, diabetes, obesity hepatitis C, mental illness , nephrotic diseases etc); 13 - Studies on the use of remote technologies for the purpose to improve knowledge among health professionals (caregivers, nurses, doctors etc); 14 - Studies on the use of remote technologies to assess behavioral, emotional, and cognitive aspects;

REFERENCES

1. Ferrua M, Di Palma M, Fourcade A, Guillet M, Mathivon D, Puglisi V, Mir O, Minvielle E (2019) Patient experience and use of an intervention combining nurse-led telephone and technologies for the monitoring of oral cancer medication. Annals of oncology30(Suppl 5), v819 Doi: 10.1093/annonc/mdz272.011

2. Head BA, Studts JL, Bumpous JM, Gregg JL, Wilson L, Keeney C, Scharfenberger JA, Pfeifer MP (2009) Development of a telehealth intervention for head and neck cancer patients. Telemed J E Health 15(1):44-52. doi: 10.1089/tmj.2008.0061.

3. Keeney C, E, Head B, A, Myers J, Appana S, Mark P. Pfeifer (2010) The impact of a telehealth intervention on symptom burden and quality of life for head and neck cancer patients. Journal of supportive oncology; 8(5), A10-11 DOI: 10.1016/j.suponc.2010.09.019

4. Li Y, Li J, Zhan Q, He Q. A (2018) Qualitative Study of Internet Informational Support for Neck Cancer Patients. Stud Health Technol Inform 250:121-125. DOI: 10.3233/978-1-61499-872-3-121

5. Lin HY, Chen SC, Peng HL, Chen MK (2016) Effects of a case management program on patients with oral precancerous lesions: a randomized controlled trial. Support Care Cancer 24(1):275-284. doi: 10.1007/s00520-015-2787-5.

6. Matthijs de Wit L, van Uden-Kraan CF, Lissenberg-Witte BI, Melissant HC, Fleuren MAH, Cuijpers P, Verdonck-de Leeuw IM (2019) Adoption and implementation of a web-based self-management application "Oncokompas" in routine cancer care: a national pilot study. Support Care Cancer 27(8):2911-2920. doi: 10.1007/s00520-018-4591-5.

7. Ratnasekera N, Perera I, Kandapolaarachchige P, Surendra G, Dantanarayana A (2020) Supportive care for oral cancer survivors in COVID-19 lockdown. Psychooncology 29(9):1409-1411. doi: 10.1002/pon.5463.

8. Russell L, Pascoe MC, Seymour JF, Aranda S, Butow P, Gough K, Schofield P (2019) The trials and tribulations of conducting an m-health pilot randomized controlled trial to improve oral cancer therapy adherence: recommendations for future multisite, non-drug clinical trials. BMC Res Notes 12(1):226. doi: 10.1186/s13104-019-4264-6.

9. Van Der Hout A, Van De Poll-Franse L, Van Uden-Kraan C, Lissenberg-Witte B, Jansen F, De Wit M, Neijenhuijs K, Holtmaat K, Verdonck-De Leeuw I (2019) Efficacy of an e-health self-management application 'oncokompas' to support cancer survivors to obtain optimal supportive care-results of a randomized controlled trial. Supportive care in cancer 27(1), S9-S10. Doi: 10.1007/s00520-019-04813-1

10. Van Der Hout, A; Jansen, F; Lissenberg-Witte, B; De Wit, M; Holtmaat, K; Van Uden-Kraan, C; Cuijpers, P; Van De Poll-Franse, L; Verdonck-De Leeuw, I (2019) E-health self-management applications targeting cancer survivors-who do we reach? Supportive care in cancer 27(1), S200. Doi: 10.1007/s00520-019-04813-1

11. Wang HL, McMillan SC, Vijayakumar N, McDonald S, Huang LT, Gwede C, Padhya T, Russell J, Vondruska K, Buck HG, Huang Y, Visovsky C (2019) A Behavioral Physical Activity Intervention to Manage Moderate and Severe Fatigue Among Head and Neck Cancer Patients-Pre-efficacy Study in the National Institutes of Health ORBIT Model. Cancer Nurs 42(1):E1-E14. DOI: 10.1097/NCC.0000000000000568.

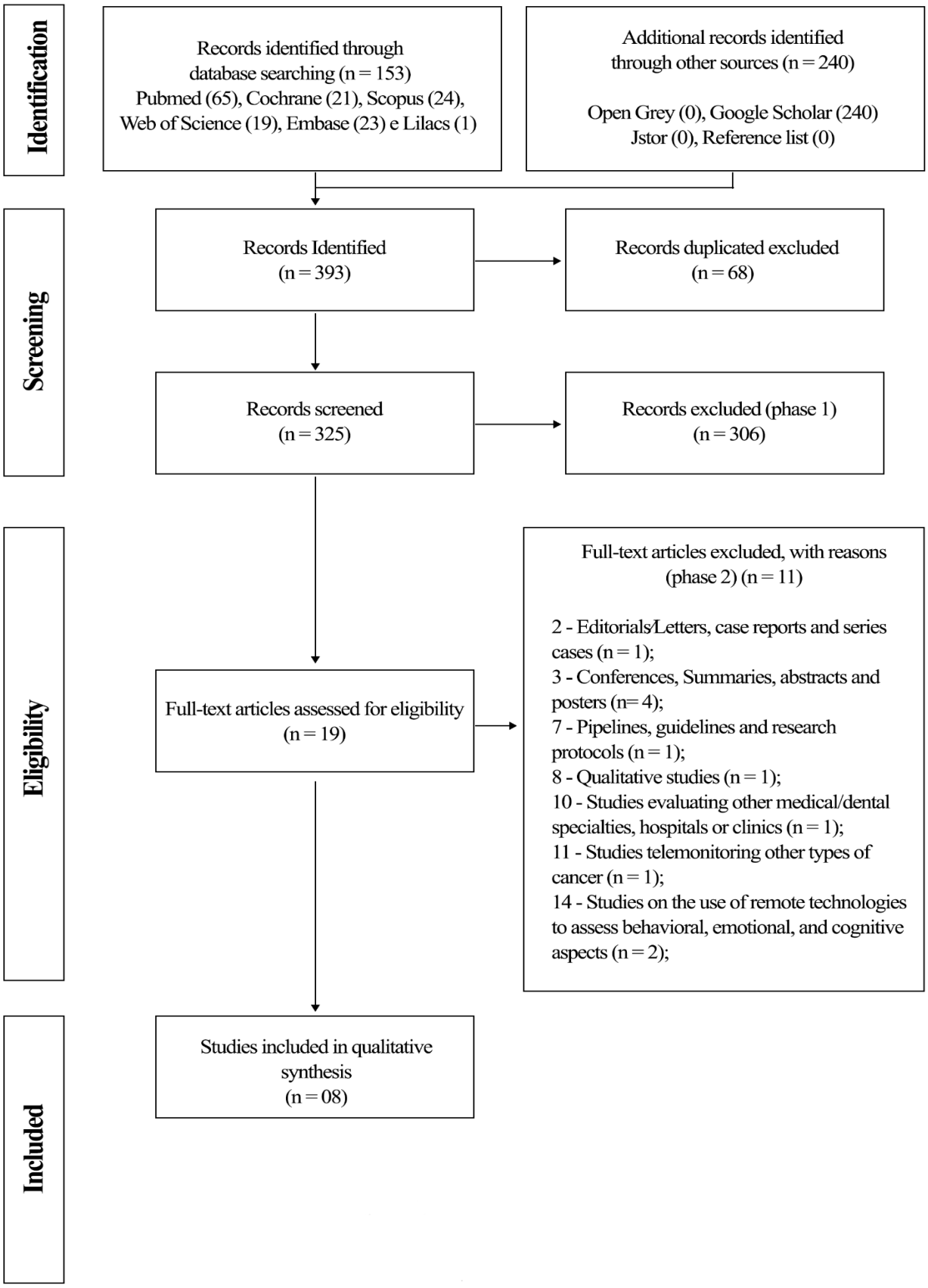

Figure. 1 - Flow diagram of the literature search and selection criteria

Table. 1 - Summary of descriptive characteristics of included articles (n=08).

Author, year, country, study design	Age in years Mean ±SD and/or Range Sex n and %	Groups		Technology tool model for telemedicine /teledentistry used;	Number of patients adhering/total group sample	Users's satisfaction with the use of the technology tool and quality of life (*P value* of r, Slope (β), RMSE, or Mean±SD)	Main conclusions
		Test (n*)	Control (n*)				
Fang et al. (2020) EUA **Clinical Trial**	Mean age 61.1±9.76 Male n = 41 (74.5%) Female n = 14 (24.5%)	55 patients	-	Web-based program, My Journey Ahead (MJA)	44 /55 patients	**Higher satisfaction levels related to:** Older age (r = 0.48, $p < 0.01$); Baseline levels of self-efficacy in coping (r=0.36, $p= 0.04$) Overall ratings of the website program (r = 0.35, $p < 0.05$); Number of logins (r = 0.40, $p= 0.02$); Minutes spent logged in to the website (r = 0.53, $p < 0.01$); Number of units viewed (r = 0.46, $p < 0.01$) **Lower satisfaction levels related to:** Higher baseline levels of cancer specific distress_ (r =-0.35, $p < 0.05$) Higher baseline levels of global distress: (r = -0.59, $p < 0.001$) Lower ratings of the website: (r = -0.48, $p < 0.01$).	The findings suggest that MJA can serve as an informative resource for HNSCC patients who are undergoing or have recently completed radiation treatment. Future studies should also incorporate appropriate strategies to address psychological distress in order to help patients thrive after treatment. Offering an easy-to-use web-based program, particularly for older patients who may have difficulty locating reliable evidence-based information on the internet, may increase information access and help address selected patient concerns.

Table. 2 (continued)

Author, year, country, study design	Age in years Mean ±SD and/or Range Sex n and %	Groups		Technology tool model for telemedicine /teledentistry used;	Number of patients adhering/total group sample	Users's satisfaction with the use of the technology tool and quality of life (*P value* of r, Slope (β), RMSE, or Mean±SD)	Main conclusions
		Test (n*)	Control (n*)				
Zini et al. (2019) Italy **Pilot study**	Patient's Age in years (44 to 59 years) Meanage 53.50 Male n = 9 (90%) Female n = 1 (10%)	10 HNC patients and 3 doctors;	-	HeNeA (Head and Neck Application)	10/11patients 3/3 doctors	**Users' satisfaction** perceived usefulness /usability (β=1, *p* =0.01, RMSE=1.97); acceptance /perceived usefulness (β=0.896, *p* =0.006, RMSE=1.67); acceptance/ usability (β=0.833, *p* =0.006, RMSE=1.41); Multiple regression analysis (predictors of acceptance) Usability (β=0.479 with *p* =0.012, RMSE=0.99) Perceived usefulness (β=0.416, *p* =0.046, RMSE=0.99) **Quality of Life** EuroQoL and symptoms severity - (β=−0.0249, *p* =0.007)	The results showed that remote symptoms monitoring via mobile app is feasible, with most of the patients complying with the requested assignments. Indeed, the compliance rate was excellent for many patients, with a median of 90% (interquartile range 50.5–100). HeNeA usability, perceived usefulness and acceptance were measured by questionnaires administered to both patients and clinicians. Patients and doctors' scores reached the pre-established thresholds.

Table. 2 (continued)

Author, year, country, study design	Age in years Mean ±SD and/or Range Sex n and %	Groups		Technology tool model for telemedicine /teledentistry used;	Number of patients adhering/total group sample	Users's satisfaction with the use of the technology tool and quality of life (*P value* of r, Slope (β), RMSE, or Mean±SD)	Main conclusions
		Test (n*)	Control (n*)				
Wang et al. (2020) Taiwan **Clinical Trial**	mean age 57.01±8.87 male n = 92 (92.0%) female n = 8 (8.0%)	Test group (mHealth app intervention) (n = 61)	Control group (routine health care and instruction) (n = 59)	mHealth app	50/61 patients	**Quality of Life** EORTC QLQ-H&N35 Baseline mean (SD), *p*= 0..37 Test group: 32.15±18.65 Control group: 28.99±(16.40) After 3 months mean (SD) *p*= 0..94 Test group: 24.91±17.13 Control group: 24.91±17.13) Overall improvement: Test group: –7.24±12.77 Control group: –4.36±10.26, *p*= 0.22	An mHealth app can significantly reduce physiological needs in postoperative oral cancer patients, and use of the mHealth app was highly accepted by patients. The main results indicated that the mHealth app can be easily incorporated into routine care of postoperative oral cancer patients to conveniently provide medical information and improve patients' self-management abilities, thereby reducing their physiological care needs and promoting better health.
Head et al. (2011) EUA **Randomized Clinical Trial**	mean age 59±11.7 male n = 39 (87.0%) female n = 5 (13.0%)	Test group (Health Buddy® app intervention) (n = 45)	Control group (routine health care and instruction) (n =35)	Health Buddy®System	42/45 patients	**Quality of Life** FACT-H&N Physical Well-being (during tx) - Spearman's rho = 0.310, *p*=0.048 Emotional Well-being (during tx) - (Spearman's rho = 0.315, *p*= 0.042)	This telehealth intervention proved to be an acceptable and feasible means to educate and support patients during aggressive treatment for head and neck cancer. Patient compliance with telehealth interventions during periods of extreme symptom burden and declining QOL is feasible if simple technology cues the patient to participate, offers positive support and relevant education, and is targeted or tailored to their specific condition.

Table. 2 (continued)

Author, year, country, study design	Age in years Mean ±SD and/or Range Sex n and %	Groups		Technology tool model for telemedicine /teledentistry used;	Number of patients adhering/total group sample	Users's satisfaction with the use of the technology tool and quality of life (*P value* of r, Slope (β), RMSE, or Mean±SD)	Main conclusions
		Test (n*)	Control (n*)				
Pfeifer et al. (2015) EUA **Radomized Controlled Trial**	Male n = 69 (86.25%); Female n = 11 (13.75%) Gender p = 0.048 test group: male n = 39 (87.1%) control group: male n = 30 (85.1%) Mean age ±SD p = 0.020 test group: male 60.73±10.2 control group: male 59.67± 11.8	Test group (Telehealth device intervention) (n = 48);	Control group (Routine health care and instruction) (n = 38)	Health Buddy®System	45/48 patients	**Quality of Life** During treatment PWB (*p*= 0.001) After treatment PWB (20.6 [SD, 12.1] vs 17.0 [11.7]; *p*= 0.021), No significance statistic - after treatment EWB (18.04 control vs 18.75 test, *p*= 0.250) SWB (21.91 control vs 23.21 test, *p*= 0.477) FACT-HN (89.86 control vs 101.53 test, *p*= 0.103)	Data analyses revealed that patients who were treated for head and neck cancer and were exposed to a simple telehealth intervention reported significantly better QoL and a lower symptom burden post treatment compared with patients who received routine cancer care.

Table. 2 (continued)

Author, year, country, study design	Age in years Mean ±SD and/or Range Sex n and %	Groups		Technology tool model for telemedicine /teledentistry used;	Number of patients adhering/total group sample	Users's satisfaction with the use of the technology tool and quality of life (*P value* of r, Slope (β), RMSE, or Mean±SD)	Main conclusions
		Test (n*)	Control (n*)				
van der Hout et al. (2019) **/** van der Hout A et al (2020) Netherlands **Non-blinded, randomised, controlled trial**	Age - Mean (SD): test group 65(56–71) control group 65 (57–71) Women test group n= 158 (49%) control group n= 158 (52%) Men test group n = 162 (51%) control group n = 147 (48%)	Test group (direct access to Oncokompas) 99 (31%)	Control group (access to Oncokompas after a waiting period of 6 months) 86 (28%)	eHealth application Oncokompas	59 /99 patients	**Quality of Life** 6 months follow-up (test group) Mean±SD: 60.0±13.7 HRQOL: 2.3 [95% CI 0.0–4.5*p*=0.048] **Higher HRQOL levels related to:** Personal factors (LMM analysis; F (3,df) - three-way interaction) Self-efficacy F (3,1487) =2.903, *p*= 0.034; Personal control F (3,1481)=3.478, *p*= 0.015; Health literacy F (3,1478)=2.869, *p*= 0.035; HRQOL F(3,1617)= 0.903, p= 0..44;	Oncokompas did not improve knowledge, skills, and confidence for self-management or other secondary outcome measures such as supportive care needs. Only secondary outcomes of HRQOL and tumour-specific symptom burden were improved.

Table. 2 (continued)

Author, year, country, study design	Age in years Mean ±SD and/or Range Sex n and %	Groups		Technology tool model for telemedicine /teledentistry used;	Number of patients adhering/total group sample	Users's satisfaction with the use of the technology tool and quality of life (*P value* of r, Slope (β), RMSE, or Mean±SD)	Main conclusions
		Test (n*)	Control (n*)				
Duman-Lubberding et al. (2020) Netherlands **pretest-posttest design**	Mean age59.05±9.85 Male n = 34 (60.7%) Female n = 22 (39.3%)	56 HNC patients	-	eHealth application Oncokompas	56/68patients	Satisfaction - (mean score ± SD) Mean satisfaction score (7.3±1.5) General (60.4 %, 6.8±1.2) User-friendly (76.0 %, 7.1±1.6) Use without assistance (90.6 %, 7.8±1.7). NPS +1.9 Satisfaction not significantly associated HRQOL (*p*= 0.0.35).	OncoKompas is considered feasible, but the results also show that improvements can be made to enhance the feasibility and increase the satisfaction among cancer survivors. The PROs can be further investigated and possibly be reduced. It is worthwhile to obtain more insight into how further tailoring of eHealth applications and more sophisticated marketing strategies can be applied leading to applications that are attractive to more participants and hereby increase adoption and usage.

Table 1 subtitles: HNC=Head and neck cancer; MJA=My Journey Ahead; HNSCC=Head and Neck Squamous Cell Carcinoma; RMSE=Root mean squared error; EuroQoL=EQ-5D Questionnaire; EORTC QLQ-H&N35=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 and Head and Neck Module; PWB=Physical Well-Being; EWB=Emotional Well-Being; SWB= Social Well-Being; FACT-HN=The Functional Assessment of Cancer Therapy-Head & Neck Scale; HRQOL= Health-related Quality of Life; NPS= Net Promoter Score.

Table. 3 - Evaluation of methodological quality according to the design of the randomized studies (n=3)

Study	Methodological quality assessed[a]													Methodological quality[b]
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	
Anja van der Hout (2019)/ Anja van der Hout (2020)	Y	Y	Y	N	N	U	Y	U	Y	Y	Y	N	Y	Moderate
Head (2011)	N	N	N	N	N	N	N	N	N	N	Y	Y	N	Low
Pfeifer (2015)	N	N	Y	N	N	U	Y	U	Y	Y	Y	Y	Y	Moderate

Note: [a]For Randomized Controlled Trials - Q1. Was true randomization used for assignment of participants to treatment groups? Q2. Was allocation to treatment groups concealed? Q3. Were treatment groups similar at the baseline? Q4. Were participants blind to treatment assignment? Q5. Were those delivering treatment blind to treatment assignment? Q6. Were outcomes assessors blind to treatment assignment? Q7. Were treatment groups treated identically other than the intervention of interest? Q8. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed? Q9. Were participants analyzed in the groups to which they were randomized?Q10. Were outcomes measured in the same way for treatment groups? Q11. Were outcomes measured in a reliable way?Q12. Was appropriate statistical analysis used? Q13. Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?

[b]Low quality: 1 to 5 ”yes” answers; Moderate quality: 6 to 10 ”yes” answers; High quality: 11 to 13 ”yes” answers;

Abbreviations: N, no; U, unclear; Y, yes

CAPÍTULO 4 - THE USE OF ARTIFICIAL INTELLIGENCE TOOLS IN CANCER DETECTION COMPARED TO THE TRADITIONAL DIAGNOSTIC IMAGING METHODS: AN OVERVIEW OF THE SYSTEMATIC REVIEWS

Silva HECD, Santos GNM, Leite AF, et al. The use of artificial intelligence tools in cancer detection compared to the traditional diagnostic imaging methods: An overview of the systematic reviews. *PLoS One*. 2023; 18(10):e0292063. Doi:10.1371/journal.pone.0292063

4.1 ABSTRACT

Background and purpose:
In comparison to conventional medical imaging diagnostic modalities, the aim of this overview article is to analyze the accuracy of the application of Artificial Intelligence (AI) techniques in the identification and diagnosis of malignant tumors in adult patients.
Data sources: The acronym PIRDs was used and a comprehensive literature search was conducted on PubMed, Cochrane, Scopus, Web of Science, LILACS, Embase, Scielo, EBSCOhost, and grey literature through Proquest, Google Scholar, and JSTOR for systematic reviews of AI as a diagnostic model and/or detection tool for any cancer type in adult patients, compared to the traditional diagnostic radiographic imaging model. There were no limits on publishing status, publication time, or language. For study selection and risk of bias evaluation, pairs of reviewers worked separately.
Results: In total, 382 records were retrieved in the databases, 364 after removing duplicates, 32 satisfied the full-text reading criterion, and 09 papers were considered for qualitative synthesis. Although there was heterogeneity in terms of methodological aspects, patient differences, and techniques used, the studies found that several AI approaches are promising in terms of specificity, sensitivity, and diagnostic accuracy in the detection and diagnosis of malignant tumors. When compared to other machine learning algorithms, the Super Vector Machine method performed better in cancer detection and diagnosis. Computer-assisted detection (CAD) has shown promising in terms of aiding cancer detection, when compared to the traditional method of diagnosis.
Conclusions: The detection and diagnosis of malignant tumors with the help of AI seems to be feasible and accurate with the use of different technologies, such as CAD systems, deep and machine learning algorithms and radiomic analysis when compared with the traditional model, although these technologies are not capable of to replace the professional radiologist in the analysis of medical images. Although there are limitations regarding the generalization for all types of cancer, these AI tools might aid professionals, serving as an auxiliary and teaching tool, especially for less trained professionals. Therefore, further longitudinal studies with a longer follow-up duration are required for a better understanding of the clinical application of these artificial intelligence systems.
Systematic review registration
Prospero registration number: CRD42022307403.
Keywords: Artificial Intelligence, Neoplasms, Cancer, Algorithm**,** Overview.

4.2 INTRODUCTION

Since early diagnosis of cancer is associated with better treatment outcomes for the patient, there is substantial interest in using artificial intelligence (AI) technology in cancer screening and detection through image recognition, in the hope of reducing diagnosis times and increasing diagnostic accuracy [1]. AI has made significant advances in fields including medicine, biomedicine, and cancer research. To forecast cancer behavior and prognosis, AI employs mathematical approaches that aid in decision-making or action based on logical and autonomous thinking and effective adaptability [2-4].

AI has the potential to dramatically affect nearly all aspects of oncology – from enhancing diagnosis to personalizing treatment and discovering novel anticancer drugs. Thus, it is important to review the recent enormous progress in the application of AI and its potential in daily clinical practice, and also to highlight limitations and pitfalls for such purpose [1,2]. Several studies have attested to the potential of AI-based techniques to predict diagnosis, prognosis and response to treatment in some malignant tumors, including colorectal, breast, skin, and lung cancer [5-8].

Machine learning (ML), a branch of AI, has been shown to minimize intercurrences in dysplasia and cancer categorization, assuring uniformity and validity, and influencing treatment decisions [9]. Progress in Deep Learning (DL) approaches has shown gains in image-based diagnosis and illness detection in the study of cancer and oncology [10,11]. DL configurations are non-linear layered artificial neural networks that are hierarchically coupled. A range of DL architectures based on input data types have been developed during the last few years. Simultaneously, the model's performance was evaluated, and it was discovered that the use of DL in cancer prediction is superior than the standard procedures employed in ML [12].

In this context, these systems offer a lot of potential to support and enhance diagnostic methods, such as overcoming the limitations of human memory and attention, improving the effectiveness of computations and interpreting data, and preventing biases and prejudices from influencing judgments. However, radiologists find it challenging to assimilate and evaluate a significant volume of data to perform diagnosis and therapy because of the enormous volume and complexity of the

picture data. The diagnosis takes longer, there is a higher risk of mistakes, and radiologists are prone to become fatigued. Automation in the field of radiological imaging can help to solve a number of issues, including a) improving the accuracy and precision of picture analysis [13]; b) reducing interobserver variability [14]; and c) increasing the speed of image analysis and reports [15,16]. Thus, medical analysis demands the evolution of automated decision-making systems, with the aid of the use of computational intelligence for fast, accurate and efficient diagnosis [17], prognosis and treatment of diseases, such as brain tumors [18].

AI models, such as artificial neural networks (ANNs), have been popular in diagnostic and predictive decision-making procedures when clinical situations are complicated, such as liver cancer [19], malignant melanoma and breast cancer [20,21], and colon cancer [22]. Image processing, pattern recognition, artificial intelligence, and medical pictures are all combined in Computer-Aided Diagnosis (CADs) systems. Several computer-based solutions, such as Computer Aided Diagnosis (CADx) or Computer-Aided Detection (CADe), have been suggested to aid the radiologist in the process of interpreting computed tomography (CT) scans. CADe systems may detect and label suspicious regions as lesions in an image, while CADx systems not only highlight suspicious areas, but also point out the nature of the detected lesion as malignant or benign [23,24]. Therefore, CAD systems might potentially decrease the workload of radiologists, leading to fast and accurate diagnoses.

The terms computer-aided detection (CADe) and computer-aided diagnosis (CADx) are frequently used to describe CAD in the literature. By calling radiologists' attention to questionable areas in an image, CADe schemes aim to eliminate observational oversight. On the other hand, CADx strategies aim to classify a worrisome area and characterize it. CAD schemes and ML-based prediction models for medical images, such as breast imaging, for example, have limited therapeutic relevance despite significant research efforts and the availability of marketed CAD solutions [25]. Radiomics, on the other hand, is a discipline that has emerged as a result of the recent quick breakthroughs in bioinformatics and the introduction of high-performance computers. Radiomics includes calculating numerical image-based features that can be mined and applied to forecast clinical outcomes [26]. To measure and define the size, shape, density, heterogeneity, and texture of the targeted tumors in medical imaging, radiomic techniques are utilized to extract a

large number of features from a series of medical images [27]. Segmenting the tumor region and extracting features from there is one way to guarantee that the derived features have some clinical value. As a result, manual or partially automated tumor segmentation is used in several radiomics-based systems. New methods for creating CAD schemes are also being investigated and described in the literature due to the increasing enthusiasm for deep learning-based artificial intelligence (AI) technology [28]. Numerous research have contrasted CAD schemes employing deep learning techniques and traditional radiomics to examine their benefits and drawbacks [29, 30].

Since deep learning models can directly extract characteristics from medical images, DL-based CAD schemes are appealing [31]. However, despite the difficulty in achieving high scientific rigor when creating AI-based deep learning models [32], using AI technology to create CAD schemes has emerged as the research standard. Aside from cancer detection and diagnosis, new AI-based models are being broadened to incorporate extensive clinical applications such short-term cancer risk and prognosis prediction and clinical outcome.

Currently, despite systematic reviews on the subject, there is still no overview in the literature that brings together the knowledge of published systematic reviews regarding the use of artificial intelligence in cancer detection in a single publication.

Considering the current potentialities of the aforementioned AI-driven systems for the oncologic field, the capability of these systems to detect malignant tumors based on different imaging modalities should be investigated. Therefore, this overview article aims to answer the following question: When compared to standard imaging diagnosis, how accurate are artificial intelligence applications for cancer detection in adult patients?

4.3 MATERIALS AND METHODS

Protocol Registration

The protocol of this study was registered on the International Prospective Register of Systematic Reviews - PROSPERO (www.crd.york.ac.uk/PROSPERO/)

under number CRD42022307403. This overview was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses, following the PRISMA checklist (http://www.prisma-statement.org/) and was developed according to the JBI Manual for Evidence Synthesis (https://synthesismanual.jbi.global) and the Cochrane Handbook for Systematic Reviews (www.training.cochrane.org/handbook).

The definition of systematic reviews considered was that established by the Cochrane Collaboration. A study was considered a systematic review when reporting or including:

i) research question;

ii) sources that were searched, with a reproducible search strategy (naming of databases, naming of search platforms/engines, search date and complete search strategy);

iii) inclusion and exclusion criteria;

iv) selection (screening) methods;

v) critically appraises and reports the quality/risk of bias of the included studies;

vi) information about data analysis and synthesis that allows the reproducibility of the results; [33,34]

Search Strategy

On January 21th, 2022, a broad search of articles without language or time limits was performed in the following databases: PubMed, Cochrane Central Register of Controlled Studies (Cochrane), SciVerse Scopus (Scopus), Web of Science, Latin American and Caribbean Health Sciences (LILACS), Excerpta Medical Database (Embase), Scientific Electronic Library Online (Scielo), Business Source Complete (EBSCOhost) and grey literature through Proquest, Google Scholar and JSTOR. The following Medical Subject Headings (MeSH) terms "Cancer Early Diagnosis," "Artificial Intelligence," "remote technology," "neoplasm" and synonyms were used to develop the search strategy and acquire the main strategy in PubMed. When words with different spelling appeared, synonyms that were in the MeSH terms were used. This strategy was adapted for the other databases. The search strategy used is in S1

Table. Manual searches of reference lists of relevant articles were also performed.

Immediately after literature search, the references were exported to reference manager online Rayyan QCRI (https://rayyan.qcri.org/welcome) and duplicated references were removed.

Inclusion And Exclusion Criteria

PIRDs (Participants, Index test, Reference Test, Diagnosis of Interest and **S**tudies) acronym was used to define inclusion and exclusion criteria. As inclusion criteria, diagnostic models and/or detection tool of any type of cancer in adult patients (P) in systematic reviews using AI (I) compared to the traditional model of diagnostic radiographic imaging (R) were evaluated. For the diagnoses of interest (D), the following accuracy metrics for detecting and diagnosing cancer were considered: sensitivity, specificity, Receiver Operating Characteristic (ROC) curve, and Area Under the Curve (AUC).

Exclusion criteria comprised: 1 - Studies evaluating diagnosis of areas other than medicine and dentistry (Physiotherapist, Nutritionist, Nursing, Caregivers etc.); 2 – Patients with a confirmed diagnosis of cancer; 3 - Systematic Reviews on AI, ML, DL and CNN not evaluating the diagnostic accuracy of the systems; 4 - Systematic Reviews with AI use for other diseases diagnosis (Diabetes, Hypertension, etc); 5 - Systematic reviews in which AI was not compared to a reference test; 6 - Systematic reviews evaluating other technologies for detection or cancer diagnosis (spectrometry, biomarkers, autofluorescence, Multispectral widefield optical imaging, optical instruments, robotic equipment etc.); 7 - literature reviews, integrative reviews, narrative reviews, overviews; 8 - Editorials/Letters; 9 - Conferences, Summaries, abstracts and posters; 10 - In vitro studies; 11 - Studies of animal models; 12 - Book chapters; 13 - Pipelines, guidelines and research protocols; 14 - Review papers that, despite self-styled systematic reviews, do not fulfill the criteria for the definition of Systematic Reviews; 15 - Primary studies of any type.

Data Extraction

The studies selection was performed in two phases. On phase 1, two independent reviewers (HECS and GNMS) evaluated titles and abstracts of all records, according to the eligibility criteria. On phase 2, both reviewers (HECS and GNMS) independently read the full texts according to the inclusion and exclusion criteria. In case of disagreements, both reviewers discussed and, if consensus was not reached, a third reviewer (AFL) was consulted to reach a final decision. At phase 2, the articles were excluded if they did not fulfill the key characteristics of systematic reviews according to the following criteria [33,34]:

1) Those carried out by a single reviewer

2) Those who do not propose a specific research question (e.g., using PICOS or another appropriate acronym);

3) Those who do not determine pre-specified eligibility criteria;

4) Those who do not use a pre-specified search strategy;

5) Those who do not apply the search strategy to at least two databases

6) Those that do not provide a clear description of the study selection process (methods used to include and exclude research at each level);

7) Those who do not use any method (qualitative/narrative or quantitative using instruments) to assess the methodological quality of included studies.

Study Selection

Data extraction was also performed by two independent reviewers (HECS and GNMS) and crosschecked. Extracted data comprised: Author, year, country; Design of included studies; N of included Studies/ N of select studies; Type of cancer; Index test; Reference test; True positives / N of images; True Negatives /N of images; Sensitivity and Specificity/ odds ratio Mean±SD, *p-value*; Diagnostic accuracy; and main conclusions of each paper. When necessary, request for additional information, via email, was made to the authors of the selected articles. Three authors did not provide consolidated data in the form of quantitative analysis. Despite contact via

email and social networks, there were no responses from any of the three authors [35-37].

Assessing The Methodological Quality Of Included Studies

The Critical Appraisal checklist for Systematic Reviews (Joanna Briggs Institute, 2014) was used to assess the methodological quality of the studies independently by two reviewers (HECS and GNMS) [38]. It should be noted that critical appraisal/risk of bias tools classically indicated for systematic reviews, such as AMSTAR 2 and ROBIS, were designed for systematic reviews of intervention, while the articles included were systematic reviews of diagnostic accuracy. We opted for performing the methodological assessment, not the risk of bias in the selected studies.

Studies were characterized according to the scoring decisions agreed by reviewers previously. Systematic Reviews were considered of “low” methodological quality when only 1 to 4 tool items received “yes” answers; “moderate” quality with 5 to 8 “yes” answers; and “high” quality with 9 to 11 “yes” answers.

Considered Outcomes

The indexes and reference tests were compared concerning to cancer detection and diagnosis (sensitivity, specificity, ROC, AUC). Despite previously planned on the protocol, meta-analysis of the data was unfeasible due to studies’ high methodological heterogeneity.

4.4 RESULTS

Description Of Included Studies

The electronic search of five databases and grey literature retrieved 382 records. Removal of 18 duplicated studies resulted in 364 records. Titles and abstracts from these studies were read and those not fulfilling the eligibility criteria were excluded. In addition, 40 records retrieved from grey literature were considered. At the end of phase 1, 32 papers remained for full text reading (phase 2). Manual search of reference lists did not provide additional studies. Full text reading resulted in 09 eligible studies for qualitative analysis. S2 Table presents excluded articles and reasons for exclusion. A flowchart of the complete process inclusion is shown in Fig 1.

Fig 1. Flow diagram of the literature search and selection criteria

Included studies were conducted in EUA [28], Netherlands [36], Italy [40], Sweden [35], China [41,42], Indonesia [43], United Kingdom [44] and Denmark [37]. All included studies were published in English. One SR included descriptive studies [39], three RS included diagnostic accuracy studies [40,43,44], four SR included prospective or retrospective studies [35,36,41,42] and one SR included clinical trial studies [37]. The accuracy of AI for detecting cancer in adult patients was evaluated by sensitivity, specificity, ROC, and AUC.

Table 1 summarizes study details regarding participants, index test, reference test, outcomes (true positive, true negative, sensitivity, specificity and diagnostic accuracy) and conclusions.

Methodological Quality Within Studies

None of the studies fulfilled all methodological quality criteria. However, five studies [39-42,44] were considered of “high” methodological quality, three studies [35,37,43] were of “moderate” methodological quality and only one study [36] was

considered of “low” methodological quality.

In two studies [36,44], the review question was not considered clearly and explicitly stated. The inclusion criteria was not appropriate for the review question in one study [36], the sources and resources used to search for studies was not adequate in one study [39], the likelihood of publication bias was not assessed in four studies [35, 36,37,39], the recommendations for policies and/or practices supported by the reported data were unclear for a study [37], and the specific directives for new research were inconclusive for three studies [36,37,41]. In all of studies the search strategy and the criteria for appraising studies were appropriate.

More information about the methodological quality assessment of included studies can be find in Table 2 (summarized assessment).

Results Of Individual Studies

The systematic review conducted by the Department of Radiology at the University Medical Center Groningen in the Netherlands, looked at computer-assisted detection (CAD) in breast MRI and evaluated radiologists' accuracy in distinguishing benign from malignant breast lesions. Of the 587 papers assessed by the study authors, the 10 studies selected by eligibility criteria included a total of 895 patients with a total of 1264 breast lesions. Sensitivity and specificity were used to compare the performance accuracy of radiologists with and without CAD. Radiologists with experience attained a non-CAD sensitivity of 89% and a CAD sensitivity of 89%, respectively. On the other hand, the specificity was 86% without CAD and 82% specificity with CAD, respectively. Residents' sensitivity rose from 72% to 89% with CAD, while the difference was not statistically significant. In terms of specificity, the findings without CAD 79% and with CAD 78% were identical. The CAD in breast MRI has little bearing on the sensitivity and specificity of competent doctors. [39].

The reviewers from Universitas Gadjah Mada in Indonesia conducted a systematic review to establish the diagnostic accuracy of various ML algorithms for calculating breast cancer risk. There were 1,879 publications assessed in total, with 11 being included in systematic review and meta-analysis. Super Vector Machine

(SVM), Artificial Neural Networks (ANN), Decision Tree (DT), Naive Bayes (NB), and K-Nearest Neighbor were identified as five types of ML algorithms used to detect breast cancer risk (KNN). The AUC of the Summary Receiver Operating Characteristic (SROC) for the SVM method was > 90%, demonstrating the greatest performance among the algorithms studied in terms of calculating the risk of breast cancer, and thus having the best precision value compared to other machine learning algorithms [43].

The systematic review carried out by researchers from the University College London, United Kingdom, searched the literature for evidence of the effectiveness of a CAD systems in cancer imaging to assess their influence in the detection and diagnosis of cancer lesions by radiologists. A total of 9,199 articles were reviewed, of which 16 papers with radiologists using CAD to detect lesions (CADe) and 32 papers with radiologists using CAD to classify or diagnose lesions (CADx) were included for analysis. CADx was observed to significantly improve diagnosis in mammography, with a diagnostic odds ratio (DOR) value of 4.99 (0.53), with an average increase of 8 and 7% between without and with CADx for sensitivity and specificity, respectively; and for the breast ultrasound DOR was 4.45 (1.40), with a mean increase of 4 and 8% for sensitivity and specificity, respectively. In cases where CADx were applied to pulmonary CT, DOR was 2.79 (1.45) and to dermatological images DOR was 3.41 (1.00). It was found diagnostic contradictions with a mean decrease in specificity on pulmonary CT of 7% and on dermatological images of 17%. There was no evidence of benefit from using CADe. The review showed that CADx may offer some benefit to radiologists in specific imaging applications for breast cancer diagnosis although there is no evidence that it can be used in a generalized way, suggesting its application in some types of cancer diagnosis [44].

Based on a study of the current literature, reviewers from Sichuan University in Sichuan, China, conducted a meta-analysis to determine the accuracy of CAD for thyroid nodule diagnosis. A total of 1,206 publications were screened, with 5 of them being chosen for systematic review and meta-analysis in a set of 536 patients and 723 thyroid nodules. The CAD system's sensitivity in diagnosing thyroid nodules was 0.87, which was comparable to expert radiologists' 0.88. However, the CAD system had lower specificity of 0.79 and DOR of 25 when compared to specificity of 0.92 and DOR of 86 of experienced radiologists. The CAD system has potential as an auxiliary tool in decision making, being a possible ally of radiologists in the diagnosis of thyroid

nodules [42].

The accuracy and recall rates (RR) of single reading (SR) vs SR + CAD and double reading (DR) vs SR + CAD were examined in a systematic study undertaken by authors from Metropolitan University College in Copenhagen, Denmark. They looked at 1,522 papers of which 1,491 were excluded by abstract. Of the remaining 31 articles, 18 were excluded after full text reading, and therefore 13 matched the review's inclusion criteria. Except for two publications in the SR vs. SR + CAD comparison, adding CAD increased sensitivity and/or cancer detection rate (CDR). There were no significant variations in sensitivity or CDR between the DR group and the SR + CAD group. In all but one research, adding CAD to SR raised RR and lowered specificity. Only one study found a significant difference between the DR and SR+CAD groups. To assess the efficacy of CAD, more research is needed based on coordinated population-based screening programs with extended follow-up times, high-volume readers, and digital mammography [37].

Researchers from Lund University, Skne University Hospital Malmö, Sweden, conducted a systematic review to verify whether readings of mammographic images by a single breast radiologist plus CAD were at least as accurate as readings by two breast radiologists. The authors looked over 1,049 papers of which 996 were excluded. 53 full-text articles were assessed for eligibility and only four met the inclusion criteria, with a population of 271,917 women being investigated. The findings suggested that there was inadequate scientific evidence to establish whether a single mammography reading by a breast radiologist plus CAD is as accurate as the present method of double reading by two breast radiologists. Similarly, the scientific evidence in the literature was insufficient to investigate cost-effectiveness, and the study's quality was deemed low [35].

Authors from the Italian University of Naples "Federico II" conducted a systematic evaluation to assess the diagnostic accuracy of ML systems for diagnosing prostate cancer (csPCa) using magnetic resonance imaging. After the final editing, a total of 3,224 articles were evaluated, of which 3,164 were excluded. Thus, 60 full-text articles were blindly evaluated by each investigator for eligibility, with 12 articles included, with a total of 1979 imaging screenings evaluated. As in the general analysis, statistical heterogeneity was considerable in all subgroups. In the identification of csPCa, the overall AUC for ML was 0.86. The AUC for the biopsy subgroup was 0.85. The AUC for the radical prostatectomy subgroup was 0.88 and

Deep learning had an AUC of 0.78. The systematic review presents promising results for the quantitative identification of csPCa based on ML, with the potential to generate improvements in the detection of csPCa in terms of accuracy and reproducibility in clinical practice [40].

The diagnosis accuracy of CAD systems based on magnetic resonance imaging for PCa was investigated in a systematic review conducted by Gansu University of Traditional Chinese Medicine in China. A total of 3107 articles were examined. Of these, 3070 were excluded and of the remaining 37 articles, 15 were included for analysis with a total of 1945 patients. The overall sensitivity of the CAD system varied from 0.47 to 1.00, with specificity ranging from 0.47 to 0.89, according to the meta-analysis. The CAD system's sensitivity was 0.87, specificity was 0.76 and AUC was 0.89. Among the CAD systems, the SVM exhibited the best AUC, with sensitivity ranging from 0.87 to 0.92 and specificity ranging from 0.47 to 0.95. In terms of prostate zones, the CAD system exhibited the highest AUC in the transitional zone, with sensitivity ranging from 0 to 1. The review points out the advantage of using CAD systems for prostate cancer detection due to its high sensitivity and specificity, and the best performance of SVM algorithm for the aforementioned detection purpose [41].

The authors of a systematic review undertaken by the University of Alabama at Birmingham (UAB), Birmingham, AL, USA, analyzed the most current studies in the classification of gliomas by radiomics based on machine learning, evaluating the clinical utility and technical flaws. At the end of the screening phase, a total of 2858 patients were analyzed, from 18 articles that were chosen from 1177 publications, with 1159 papers excluded in the selection process according to the eligibility criteria adopted. The results were promising for predicting the quality of MRI images using radiomics approaches. However, there was no consensus on the radiomics pipeline, considering that the selected articles have employed a wide range of software, large amount of extracted features, different sequences and machine learning techniques. As a result, the authors urge that more standardized research should be done before radiomic glioma categorization is used in clinical practice [36].

Certainty Of The Evidence In The Systematic Review's Included

Only two articles [35,41] used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method to assess the evidence, which examines five factors: risk of bias, indirectness, inconsistency, imprecision, and publication. Due to the risk of bias and inconsistency, one paper [41] discovered low quality evidence for the following outcomes: true positives (patients with prostate cancer), true negatives (patients without prostate cancer), false negatives (patients incorrectly classified as not having prostate cancer), and false positives (patients incorrectly classified as having prostate cancer).

The second systematic review [35] evaluated only one study regarding the certainty of evidence for the following outcomes: Cancer detection rate and Recall rate, and the quality of the evidence found was very low due to the risk of bias and Indirectness.

Overlapping

Within the RS reviews, included in this overview, a total of 136 primary studies were found. Approximately 3.67 % of these main studies were included in multiple SRs. Only five studies were mentioned more than once. S3 Table provides more details on the overlap and features of the primary studies.

4.5 DISCUSSION

To the best of the authors' knowledge, this is the first overview article that critically appraise the scientific evidence of AI use for detecting and diagnosing malignant tumors on different imaging modalities. As this is a current and relatively novel topic, nine recent published SRs were retrieved in the literature search. These SRs found high accuracy metric results for the aforementioned diagnostic purpose, demonstrating the potential of AI tools for the oncologic field. The selected studies

demonstrated the use of computer-assisted detection (CAD) [35,37,39,41,42,44], machine learning algorithms [40,41,43]and radiomic analysis [36] for detection and diagnosis of malignant tumors based on radiological images.

AI-driven methods for detecting and diagnosing cancer were analyzed by accuracy metrics, such as sensitivity, specificity, AUC, and ROC. The SVM algorithm showed better performance in the detection and diagnosis of prostate cancer and breast cancer when compared to other machine learning algorithms [41,43]. In four studies, CAD systems demonstrated some benefit in helping to detect cancer [39,41,42,44]. Nevertheless, the use of this tool did not present evidence that it can be used in a generalized way, with better indication for some types of cancer, such as breast cancer [44]. In addition, two studies found promising evidence on the use of ML and radiomic analysis in prostate cancer detection and glioma classification, with potential applicability in clinical practice [36,40].

Two questions that were often addressed in the selected articles were which professional can benefit most from the use of AI systems and how these tools should be used. The CAD systems demonstrated high values of sensitivity and sensitivity for diagnosing prostate cancer and this performance may be related to the location of the tumor in the prostate, for example, central gland, peripheral zone and transition zone. It was observed that the sensitivity and specificity in the transition zone was higher than in the peripheral zone and in the central gland [41]. Some papers corroborate the findings that radiologists benefit most from the use of CAD systems in the detection of prostate cancer lesions [45-48].

However, in other study, less experienced radiologists benefited more from the use of artificial intelligence than experienced professionals [39]. Residents or radiologists with little or no experience had greater sensitivity when accompanied by a CAD system for discriminating between breast lesions on MRI. On the other hand, the performance of experienced radiologists showed a non-significant decrease in specificity from 86% (95% CI: 79–91%) without CAD to 82% (95% CI: 76–87%) with CAD. This observation is due to the fact that CAD systems are based only on the dynamics of enhancement, without considering the morphology of the lesion, which suggests that experienced radiologists may be misled by the enhancement pattern of CAD, resulting in decreased specificity [39]. The literature agrees with the findings that less experienced radiology professionals and residents benefit most from the use of CAD systems in the detection of lesions. [49-52]. Another study demonstrated

that when evaluating thyroid nodules for malignancy using ultrasound imaging, a CAD system had similar sensitivity and negative likelihood ratios compared to experienced radiologists [42].

Two studies [35,37] found no significant evidence regarding sensitivity, specificity, and diagnostic accuracy, between single-reading or double-reading mammography compared with single-reading plus CAD or double-reading plus CAD. The use of CADe to detect lesions on images added less value to radiologists than CADx, used to diagnose lesions, with a small increase in weighted mean sensitivity but a decrease in mean specificity However, CADx did not improve diagnosis in combined mammography and breast ultrasound systems. Thus, CADx can be help radiologists that are looking for breast cancer in mammograms or ultrasounds, but it cannot be assumed that its use may be generalized, with applications in other types of cancer [44].

The literature is still controversial regarding the issue of single reading with the presence of CAD and double reading. A previous study found equivalent performance of CAD systems when a single reading was compared to double reading in the detection of cancer lesions [53]. However, for detecting pulmonary nodules, the performance of a CAD system was comparable to a second opinion reading [54]. However, there are works that demonstrate that the single reading of a reader with the help of the CAD as a second reader produces a significantly higher sensitivity than the single reading and the simulated conventional double reading, being a valuable tool for the detection of pulmonary nodules and can be used as a second opinion reading [54]. As there are also works that attest that the independent double reading produces a better detection performance, the presence and probability of CAD mass markers can improve the interpretation of mammography [55,56].

On the other hand, a recent study stated that the quality and amount of the evidence on the use of AI systems in breast cancer screening is still far from what is needed for its incorporation into clinical practice. In screening programs, AI systems are not sufficiently specialized to take the position of radiologist double reading. Larger research do not confirm promising outcomes from smaller ones [57].

Support vector machines (SVM) exhibited the best AUC among the CAD system classifiers for the detection of prostate cancer (CaP) in magnetic resonance imaging, with a range of 0.47 to 1.00 and specificity of 0.47 to 0.89, with an AUC of

0.89 (0.86–0.91). The AUC curve demonstrated stronger sensitivity and specificity in the transition zone than in the peripheral zone and the core gland of the organ, according to the location of the tumor in the prostate. As a result, the sensitivity of different regions of the human body to screening methods may be explained. Other screening methods, with the exception of CAD-assisted MRI, may not detect it due to limited sensitivity [41].

In another study, SVM was compared to four additional classification algorithms: artificial neural network (ANN), decision tree (DT), naive bayes (NB), and K-Nearest Neighbor (KNN). In the breast cancer risk calculation, SVM was shown to generate the best area under the curve (AUC), with AUC > 90%. The SVM has a 97.13% accuracy rate, demonstrating its effectiveness in predicting and detecting breast cancer and having the greatest accuracy and low error rate. In this approach, the SVM algorithm can predict breast cancer risk and outperforms other algorithms in terms of accuracy. Different machine learning algorithms, on the other hand, can aid in the diagnosis of breast cancer. They serve to decrease the risk of errors caused by weariness or inexperienced professionals, and they allow medical data to be analyzed in less time and with more precision [43].

With a combined AUC of 0.86, machine learning paired with radiomics demonstrated excellent results in the characterization of prostate cancer (csPCa). Deep learning analyses, on the other hand, were less accurate than artisanal radiomics and non-deep ML techniques, with AUCs of 0.78 and 0.90, respectively. While deep learning excels with big datasets with hundreds or even millions of examples, this is rarely the case in medical image analytics. In this case, the datasets are often made up of hundreds of patients at most, and the artisan technique outperforms deep learning in this scenario. As deep learning is also computationally more expensive and less understandable, it should be used with caution in medical image analysis and only when it significantly outperforms alternative approaches [40].

The radiomic study of gliomas using radiomic feature extraction in conjunction with various forms of machine learning has yielded encouraging findings with high sensitivity, specificity, accuracy, and AUC. Radiomics systems that used an external dataset had AUCs of 94% and 72%, respectively, indicating a more realistic performance [35]. The ability to translate DL models into real-world applications, in order to improve acceptance and the performance of DL clinically applied by

physicians through the generalization of its applications, the interpretability of its algorithms, access to data, and medical ethics, is one of the challenges for the future of AI use in the medical field, particularly oncology, regarding the diagnosis and detection of cancer. The process of application generalization involves building a multimodal model using information other than the evaluated image itself, such as sample size, age, sex, ethnicity, incomplete data collection and a lack of a standard clinical protocol, clinical manifestations, laboratory tests, image data, and epidemiological histories. Due to the complexity of neural networks and the use of these unrepresentative datasets, overfit models that do not generalize to other populations and biased algorithms are produced [58].

The capacity of algorithms to do activities that call for intelligence is referred to as artificial intelligence. Machine learning is a subset of AI, and it refers to algorithms that learn from data in order to perform better. There are two ways that data given into an ML program may be represented: as features or as raw data. Lesion length is an example of a feature, which is a variable in data that may be measured. Digital mammography (DM), ultrasound (US), and magnetic resonance imaging (MRI) scans are examples of raw data in cancer imaging [59].

Learning features poses a challenge for these algorithms even though they often outperform handcrafted features in terms of performance. The subset of ML methods known as DL can be used to overcome this issue. The ability to recognize complicated patterns is the strength of machine learning and deep learning based approaches. Through feature engineering or feature learning, more detailed picture attributes, such as texture, form, border, location, etc., may be acquired. Higher accuracy can be achieved by segmentation based on detailed picture properties. By categorizing picture blocks of a particular size using a sliding window, typical machine learning based algorithms (such as RBFNN, SVM, etc.) get the whole segmentation image. This leads to unnecessary computation, misclassification, and jagged segmentation borders. On the other hand, deep learning-based approaches (such 3D U-Net CNN) outperform conventional machine learning-based methods in terms of performance and segmentation. Deep learning-based methods have greater discriminating abilities in pixel categorization because they can learn more useful picture attributes. However, many machine learning-based approaches require a large amount of labelled training data [59,60,61].

Features are represented in terms of other, more basic features in DL. Since DL algorithms are made up of many (deep) layers of linked neurons, they are sometimes referred to as deep neural networks (DNNs). CNNs are a specific kind of DNN. CNNs are frequently employed in cancer image analysis since they were created particularly to detect important characteristics in pictures [62,63]. Different criteria are employed for various activities in order to compare the performance of DL networks with human standards. The metrics used in categorization are founded on receiver operating characteristic analysis. AUC, accuracy, sensitivity, and specificity all have a significant impact in this situation. Thus, accuracy represents the proportion of correctly classified samples, sensitivity represents the likelihood that the model or radiologist will output a positive (and thus malignant) result if the sample is malignant, specificity represents the probability that the model or radiologist will output a negative (and thus benign) result if the sample is benign, and AUC represents the average sensitivity for all possible specificity values [60,61].

Oncologists find it challenging to comprehend how DL models assess data and make judgments since the sheer number of parameters involved make it challenging for professionals to interpret algorithms. Data access and quality are frequently negatively impacted by a deficient data sharing network, as well as competition between different institutions. Building an open data-sharing platform with the participation of numerous institutes is the first step in overcoming these challenges. Governments and businesses must create a formal structure in the future to enable secure data sharing. Examples include privacy-preserving distributed DL (DDL), which offers a way to protect privacy and enables several participants to train jointly using a deep model without explicitly sharing local datasets. Additionally, the Cancer Imaging Archive, which compiles clinical images from many hospitals and institutes, is another excellent illustration of data sharing and can support radiomic studies [58,64,65].

Due to the need to preserve patient information, which can lead to overfitting, it is challenging to get the data in sufficient quantities to have credibility in training and validation in DL. Companies handling this data must adhere to current data protection and privacy laws in both their home countries and the countries of residence of the data subjects. Before exploiting delicate data, such as genetic data, informed agreement from patients must be sought. Patients must be informed about the potential uses of their data, and it must be made sure that everyone would benefit

from them. Furthermore, thorough monitoring and validation procedures must be implemented in order to evaluate AI performance across various applications [58,64].

Before DL techniques are used in therapeutic settings, there are significant ethical issues that need to be resolved. The level of supervision needed for doctors must first be decided. Second, the party accountable for DL tools' inaccurate judgments must be identified. Before AI is implemented in real-world settings, it is also necessary to outline legal obligations in the event of a malfunction. In addition, the majority of high-end AI software works in a "black box" testing environment, meaning that users are unaware of the software's fundamental workings. The tester just knows the input/output; the reasoning behind coming to a particular conclusion is still a mystery. Clinicians frequently confront moral conundrums when making predictions without a thorough grasp of the processes underlying them, hence it is imperative to offer greater transparency in AI models by creating techniques that let users examine the details of the input data that affected the result. closer to the truth [58-65].

The main databases used in training ML and DL technologies vary according to the type of cancer. The most used ones are: Breast Cancer dataset (WBCD); Wisconsin Diagnostic Breast Cancer (WDBC); Wisconsin Prognostic Breast Cancer (WPBC) [66]; Digital Database for Screening Mammography (DDSM) [67]; The Mammographic Image Analysis Society (MIAS) [68]; Breast Cancer Digital Repository (BCDR) [69]; The Cancer Imaging Archive (TCIA) Public Access[70] and Lung Image Database Consortium – the LIDC [71]. Breast cancer databases and other databases have been reported up to date for studying cancer, but the information contained in these databases frequently presents some unfavorable issues: a) some are lacking in terms of available features (image-based descriptors, clinical data, etc.); b) others have a limited number of annotated patient cases; c) and/or the database is private and cannot be used as a reference, which makes it difficult to explore and compare performance [69]; the lack of larger datasets with manual malignancy annotations and diagnostic cancer labels constitutes the main limitation [72].

Other limitations of the databases that can be listed are: the availability of patient-based pathologic diagnoses for only a subset of cases, the inability to perform reader studies because the files do not maintain radiologists identities or a consistent ordering of radiologists marks, the interpretation of CT scans using only transaxial

images, the somewhat artificial nature of the lesion categories relative to clinical practice, the interpretation of every case is not performed by the same radiologists, and the design of the manual QA process that focus mostly on the visual identification of objective lesion annotation errors and did not analyzes inconsistencies in the subjectives lesions characteristic ratings, although the benefit of this quality assurance process to the integrity of the Database should not be understated [73].

The Critical Analysis Of Meta-Analyses That Presented Complete Data

Of the studies selected in this overview, only three studies presented meta-analyses regarding the sensitivity, specificity and diagnostic accuracy of the use of medical radiological images in the detection of cancer lesions, based on artificial intelligence tools [39, 42, 44].

Critical analysis of the meta-analysis for diagnosing thyroid nodules based on ultrasound imaging through CAD [42] showed that the CAD system had similar sensitivity and negative likelihood ratio compared to experienced radiologists. However, specificity, positive likelihood ratio and DOR were relatively low. These results indicated that there was a clear gap between the CAD system and the radiologist experienced in making the diagnosis of thyroid nodules. Furthermore, successful nodule segmentations were important and influenced the nodule recognition accuracy. Nodule malsegmentation occurred more frequently with benign nodules (n = 11, 18.6%) than with malignant nodules (n = 2, 4.7%) and the difference was statistically significant (P = 0.04). Among nodules with poor segmentation, 54.6% of benign nodules (6/11) were also diagnosed as malignant, while all malignant nodules were diagnosed as malignant. As a result, it is clear that a CAD system's subpar segmentation can raise the false positive rate while having no impact on the false negative rate. The CAD system's sensitivity to thyroid nodules was comparable to that of skilled radiologists. However, compared to an expert radiologist, the CAD system showed worse specificity and DOR. [42].

Meta-analysis for the evaluation of breast lesions with MRI showed that the combined sensitivity and specificity of the experienced radiologist remain comparable

with the implementation of CAD. Less experienced residents or radiologists seemed to achieve greater sensitivity with CAD implantation, although not statistically significant. Residents or radiologists with little or no experience obtained greater sensitivity when accompanied by a CAD system for discrimination of breast lesions on MRI. The change in sensitivity after using the CAD was not statistically significant. However, a considerable increase could be observed (72% sensitivity; 95% CI: 62–81% to 89%; 95% CI: 80–94%). This rise could be attributable to the fact that CAD alerts radiologist trainees or less skilled radiologists to more enhanced lesions, which may be helpful when assessing breast lesions with MRI. [39].

The performance of experienced radiologists showed a non-significant decrease in specificity from 86% (95% CI: 79–91%) without CAD to 82% (95% CI: 76–87%) with CAD. A clarification for this observation may be that CAD systems are based only on the dynamics of enhancement, without taking into account the morphology of the lesion. As a consequence, the use of CAD could lead to a greater number of enhanced lesions, part of which could be classified as benign based on morphology [39].

In another study using mammograms and breast ultrasound imaging in the evaluation of CAD systems, certain types of CAD offered diagnostic benefits compared to radiologists diagnosing alone: significantly better ln DOR scores were seen with CADx systems used with mammography and breast ultrasound. This fact can be observed, since the use of CADx tends to increase sensitivity and specificity in mammography (mean increase of 8 and 7% between without and with CADx for sensitivity and specificity, respectively) and breast ultrasound (mean increase of 4 and 8% for sensitivity and specificity, respectively), but adversely affects specificity in lung CT (mean reduction 7%), combined breast ultrasound and mammography systems (mean reduction 12%) and dermatologic imaging (mean reduction 17%). According to evidence, using CADe systems results in a tiny net overall drop in ln DOR as well as a similar-sized gain in sensitivity and loss in specificity [44].

It is also noticed that the use of CADx improved the diagnosis. However, the overlapping of the 95% confidence interval (CI) curves suggests that the difference is not significant. The AUC is 0.88 (SD: 0.03) for radiologists alone and 0.92 (SD: 0.03) for the same radiologists using CADx and 0.85 (SD: 0.19) for radiologists alone in studies of detection and 0.84 (SD: 0.19) for those radiologists using CADe [44].

The examined meta-analyses did, however, have several drawbacks. First, all displayed significant variation among trials in terms of sensitivity and specificity. This variability is probably due to both the fundamental variations in the patients who were included in the studies' methodologies. Second, the included studies' sample sizes were somewhat modest [39,42,44]. When conducting the meta-analyses, the authors took into account the possibility of selection [39,42,44], measurement [42], and publication [42,44] bias.

The Role Of Explainable Artificial Intelligence In DL And ML Models

Recent advances in ML have sparked a new wave of applications for AI that provide significant advantages to a variety of fields. Many of these algorithms, however, are unable to articulate to human users why they made certain decisions and took certain actions. Explanations are necessary for users to comprehend, have faith in, and manage these new artificially intelligent partners in the crucial knowledge domains of defense, medical, finance, and law for exemplo [74-76].

New ML methods including SVMs, random forests, probabilistic graphical models, reinforcement learning (RL), and DL neural networks are significantly responsible for the current strong performance of AI. These models exhibit good performance, but they are difficult to understand. In many cases, the most performing methods (such as decision trees) are the least explainable, and the most explainable methods (such as DL) are the least accurate. Explanations might be complete or incomplete. Full explanations are provided by fully interpretable models in a transparent manner. Partially interpretable models shed light on key aspects of their thought process. Contrary to black box or unconstrained models, interpretable models adhere to "interpretability restrictions" that are established according to the domain [77].

Although there may be many different types of users, frequently at various times in the development and use of the system, the Explainable Artificial Intelligence (XAI) assumes that an explanation is provided to an end user who depends on the decisions, recommendations, or actions produced by an AI system. For instance, an intelligence analyst, a judge, an operator, developers or test operators, or policy

makers. Each user group could have a particular explanation style that they find to be the most successful in conveying information [77,78].

The effectiveness of an explanation has been evaluated and measured in a number of ways, but there is presently no accepted method of determining if a XAI system is more user-intelligible than a non-XAI system. Task performance may be a more objective indicator of an explanation's efficacy than other of these indicators, such as user satisfaction. It remains an outstanding research question how to accurately and consistently measure the impact of explanations [79,80].

Before explainability can be achieved in DL models, there are still several open problems and obstacles at the intersection of ML and explanation. First, there is a lack of consensus over the terminology and many definitions used in relation to XAI. Since XAI is still a relatively new field, there isn't yet a set of accepted terms in use[81].

Second, there is a trade-off between accuracy and interpretability [82], i.e., between the thoroughness of this description and the simplicity of the information provided by the system regarding its internal functioning. This is one of the reasons why developing objective measurements for what makes a good explanation is difficult with XAI.

Utilizing findings from experiments in human psychology, sociology, or cognitive sciences to develop objectively compelling explanations is one way to lessen this subjectivity. This would allow programmers to design software for their target audience rather than for themselves, with the evaluation of these models being more concerned with people than with technology [83,84]. A promising approach to solving this problem is to combine the connectionist and symbolic paradigms [85-89]. Connectionist approaches are more exact but opaque on the one hand. Symbolic approaches, on the other hand, are more easily understood while being generally seen as less effective. Additionally, it has been demonstrated that the introduction of counterfactual explanations might aid the user in comprehending a model's conclusion [90-92].

Third, XAI approaches for DL must address the issue of delivering explanations that are understandable to society, decision-makers, and the legal system as a whole. In order to address ambiguities and establish the social right to the (not yet existing) right to explanation under the General Data Protection Regulation of all countries in general, it will be especially important to communicate

explanations that require non-technical competence [93].

It is obvious that incorporating this work into explainable AI is not an easy process. These models will need to be improved and expanded from a social science perspective in order to produce good explanatory agents, necessitating strong collaboration between explainable AI researchers and those in philosophy, psychology, cognitive science, and human-computer interaction [83].

The Use Of Uncertainty Quantification Approaches In Medical Imaging

In addition to using uncertainty quantification (UQ) approaches for medical image analysis, XAI is also used in decision-making in DL methods. Tools have been created to quantify the predicted uncertainty of a specific DL model (Abdar et al., 2021a). The implementation of a deep learning algorithm for uncertainty quantification in oncology can aid in improving performance while analyzing medical images. As a result, for exemplo, the outcomes of prostate cancer segmentation from ultrasound pictures are enhanced by the addition of uncertainty quantification [94].

Numerous advantages result from improving the application of the uncertainty quantification metric. In a medical setting, it becomes essential to identify questionable samples that require human evaluation in order to avoid silent errors that could result in incorrect diagnosis or treatments. Second, UQ makes it possible to spot the model's flaws, such as uncertain forecasts, which may point to a deficient training set. Inconsistencies in the incoming data might also be shown by a high level of UQ, which is crucial for quality control (QC). Overall, UQ strengthens user confidence in the algorithm and makes it easier for the algorithm and user to communicate. Additionally, UQ is supported by solid theoretical underpinnings and has developed as a clinically expected characteristic of an applied AI system [95]. In this situation, the model's predicted performance alone is insufficient to achieve a high level of acceptability. In order to encourage human-machine collaboration and eliminate the black-box effect, UQ is essential.

In this context, the collaboration between researchers in medicine and artificial intelligence is one future study area that might be taken into consideration. As a result, the suggested machine learning and deep learning methods can do a better

job of forecasting various diseases and cancers. This can be very beneficial for resolving uncertainties[94].

The collecting of medical data to the greatest extent possible is one of the gaps for enhancing the uncertainty metric in choices. The accuracy of the findings generated from medical picture segmentation depends heavily on the use of ground truth data. The sending of inaccurately projected facts to experts also plays a significant part in coping with uncertainty. Therefore, in the field of medical picture segmentation, there is a need for strong cooperation between researchers in medicine and computer science [94].

Big medical data collection may be a significant future direction. More data can significantly enhance the performance of several deep learning techniques. Transfer learning approaches, however, can be a good alternative if huge datasets are not available for training[94]. The majority of the UQ approaches that have been put into practice (81.15%) are based on a sampling protocol and try to produce several predictions for the same query input. The potential of deterministic UQ approaches that only require one step to compute uncertainty should be thoroughly investigated [96].

And finally, while being critical in real-world medical circumstances, the detection of Out-of-distribution (OOD) predictions using uncertainty is a subject of relatively few investigations. In an automated medical picture pipeline, input samples may show a variety of anomalies and artifacts that could interfere with the NN's performance and lead to severely inaccurate predictions. This inspires the creation of feature-based techniques designed specifically for OOD detection. Noting that OOD detection is a very active research area that is not exclusive to the UQ sector, it should be noted that OOD detection is currently not often used for medical picture analysis [96,97].

Limitations Of The Included Systematic Reviews And The Overview

Regarding the limitations presented in the systematic reviews included in this overview, it was observed: short follow-up time, which leads to an overestimated sensitivity [35] or a loss in the calculation of diagnostic accuracy measures [37]; relatively low number of studies [40]; high heterogeneity can be partly explained by

the diversity of methodological aspects, difference between patients, or diversity of techniques used [35;40;42]; presence of selection bias by choice of articles reporting sensitivity and specificity results [44], by use of retrospective studies, vaguely reported sample of patients [35], by use of studies with relatively small samples [41,42]; possible presence of publication bias due to lack of studies with unfavorable data [44]; use of digitized analog radiographs to the detriment of digital images [35,37]; behavior of radiologists in terms of training, conducting clinical tests and surveillance in the analysis. [35,44]; relatively small and old technology dataset number[35,39]; presence of measurement bias due to the large difference between the groups studied and the small number of outcomes observed in the included studies.

This overview presented as limitations: there are still few studies that use artificial intelligence, in its various approaches, in the detection of cancer, being limited to some more favorable types of cancer, such as breast cancer, prostate cancer and thyroid cancer. There is considerable heterogeneity in the methodologies of the studies, which makes it difficult to standardize the artificial intelligence technologies used. Finally, the limitation of the type and quality of images makes it difficult or impossible to use artificial intelligence in the detection of certain types of cancer, such as in the case of skin or lung cancer.

Mains research gaps and future ML/DL research directions

The fact that deep learning algorithms demand a lot of data, sophisticated imaging technology, top-tier statisticians, and research funding to produce is one of their key gaps. First of all, because of the research's existing variances in sample size, research design, data source, and imaging collecting criteria, it is challenging to quantify, integrate, and extrapolate the findings in a way that was applicable to all situations. Additionally, researchs might exhibit a significant degree of publication bias, especially when they lack external validity [98].

Furthermore, Most AI models also disregard social and cultural risk variables, and the majority of those that have been developed were built using data from the entire population. To increase the accuracy of current models' predictions and modify these tools to the unique characteristics of the population being examined, combining critical risk factors, including imaging, pathology, demographics, clinical data, smoking status, tumor histology and new and ancient technology is advised [98,99]. Researchers can create predictive models by combining several features [100,101].

The concept of multi-omics [102,103] or "Medomics" [104] is introduced as a result. Therefore, it will be worthwhile to continue to pursue the merger of various domain expertise and multidisciplinary integration.

The need for additional large-scale multicenter prospective researchs is highlighted by the fact that this type of research necessitates big datasets. Future research should concentrate on creating deep learning models from decentralized, nonparametric data [105,106]. When compared to conventional models, these methods directly process the raw data, which reduces variability while enhancing model performance [98].

However, Large datasets on the order of (tens of) thousands of patients from various medical centers are now available for research using digital mammography (DM) and digital breast tomosynthesis (DBT). Rarely does MRI research involve more than 500 individuals, and it often comes from a single center. This certainly benefits AI performance in DM and DBT research, as larger datasets and data from various sources typically result in DL models that perform better and have better generalization. Although there are currently a number of sizable retrospective and multi-reader studies for the evaluation of DL CAD systems for DM and DBT, there are less of them for ultrasound (US) and none that that are known for MRI. Thus, DL research in US and MRI needs to invest in generating larger and more diverse datasets to move from proof-of-concept models to systems ready for large multi-case studies with multiple readers, as is now the case with DM/ DBT. However, this does not mean that all DM/DBT models are sufficiently tested for implementation in clinical practice [59, 106].

In this way, sharing data between medicals center is a simple way to prevent small datasets from becoming obsolete and large ones from expanding quickly. Regulated data exchange is unfortunately a major barrier for researchers [105]. Swarm learning, where all participants contribute to both case collection and algorithm development [107,108], or even federated learning, where the data stays local but the algorithm travels [105,109,110], are positioned to solve this issue. Such methods haven't, however, been widely used up until now. The challenge of validating the precise results of DL research in cancer pictures, which is typically not achievable since the (training) data are not can be shared, is solved by the construction of checklists, showing the basic requirements for the transparent reporting AI clinical investigations. Future studies on AI will be able to be more

thorough and consistent thanks to these lists, which is necessary before they are applied broadly [59, 106].

And Finally, it is crucial to address the related ethical, medicolegal, and regulatory challenges as more AI technologies are developed that have the potential for clinical translation. There are a lot of unsolved questions on the ethical front. What situations must doctors tell their patients they're using AI techniques in their clinical workup? It might be crucial in scenarios where AI functions as a "black box," in which clinicians act on the output of an AI tool without knowing how the algorithm came to its conclusion. When an AI technology misses a cancer, who is responsible? How much should be under human control? an the DL CAD systems make final decisions? Who is responsible for bad DL decisions? Will radiologists be biased as a result of AI assistance? What are people's perceptions of DL decision tools? Can DL CAD algorithms correctly describe their thought process? Before DL models can be widely used in actual clinical settings, it is evident that there must be discussion of these algorithmic biases, which also raise ethical issues [59,106].

4.6 CONCLUSION

This overview gathered evidence from systematic reviews that evaluated the use of AI tools in the detection and diagnosis of malignant tumors based on radiographic images. The detection and diagnosis of malignant tumors with the help of AI seems to be feasible and accurate with the use of different technologies, such as CAD systems, machine learning algorithms and radiomic analysis when compared with the traditional model. ML algorithms performed better when compared to DL methods. However, these systems yielded better performance in some specific types of tumors such as cancer breast cancer, prostate cancer and thyroid nodules. Although there are limitations regarding the generalization for all types of cancer, these AI tools might aid professionals, serving as an auxiliary and teaching tool, especially for less trained professionals. Therefore, further standardized and longitudinal studies should be performed by using AI algorithms for detecting malignant lesions on different imaging modalities, by using larger datasets. These future perspectives will enable a better understanding of AI use in clinical oncologic

practice.

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Supporting information

S1 Table. Database search strategy.

S2 Table. Excluded articles and reasons for exclusion (n=23). Legend - **1 -** Studies evaluating diagnosis of areas other than medicine and dentistry (Physiotherapist, Nutritionist, Nurse, Caregivers etc.); 2 – Patients with a confirmed diagnosis of cancer; 3 - Systematic Reviews not evaluating the diagnostic accuracy Artificial intelligence, Machine learning, Deep learning and Convolutional Neural Networks; 4 - Systematic Reviews with Artificial intelligence use for other diseases diagnosis (Diabetes, Hypertension, etc); 5 - Systematic reviews in which AI was not compared to a reference test; 6 - Systematic reviews evaluating other technologies

for early detection or cancer diagnosis (spectrometry, biomarkers, autofluorescence, Multispectral widefield optical imaging, optical instruments, robotic equipment etc.); 7 - literature reviews, integrative reviews, narrative reviews, overviews; 8 - Editorials/Letters; 9 - Conferences, Summaries, abstracts and posters; 10 - In vitro studies; 11 - Studies of animal models; 12 - Thesis and Dissertations and book chapters; 13 - Pipelines, guidelines and research protocols; 14 - Review papers that do not follow the inclusion criteria adopted for the definition of Systematic Reviews; 15 - Primary studies of any type; 16 - No full paper avaliable.

S3 Table. Over Laping (n=09).

S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
PubMed	#1 - "diagnosable"[All Fields] OR "diagnosi"[All Fields] OR "diagnosis"[MeSH Terms] OR "diagnosis"[All Fields] OR "diagnose"[All Fields] OR "diagnosed"[All Fields] OR "diagnoses"[All Fields] OR "diagnosing"[All Fields] OR "diagnosis"[MeSH Subheading] OR ("diagnosable"[All Fields] OR "diagnosi"[All Fields] OR "diagnosis"[MeSH Terms] OR "diagnosis"[All Fields] OR "diagnose"[All Fields] OR "diagnosed"[All Fields] OR "diagnoses"[All Fields] OR "diagnosing"[All Fields] OR "diagnosis"[MeSH Subheading]) OR "Diagnoses and Examinations"[All Fields] OR "Examinations and Diagnoses"[All Fields] OR "Postmortem Diagnosis"[All Fields] OR "diagnoses postmortem"[All Fields] OR "diagnosis postmortem"[All Fields] OR "Postmortem Diagnoses"[All Fields] OR "Antemortem Diagnosis"[All Fields] OR "Antemortem Diagnoses"[All Fields] OR "diagnoses antemortem"[All Fields] OR "diagnosis antemortem"[All Fields] OR "Oral cancer diagnosis"[All Fields] OR "computer-aided diagnosis"[All Fields] OR "Cancer Early Detection"[All Fields] OR "Cancer Screening"[All Fields] OR "screening cancer"[All Fields] OR "non-invasive screening"[All Fields] OR "Cancer Screening Tests"[All Fields] OR "Cancer Screening Test"[All Fields] OR ("early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields] OR ("screening"[All Fields] AND "test"[All Fields] AND "cancer"[All Fields])) OR "screening tests cancer"[All Fields] OR "test cancer screening"[All Fields] OR "tests cancer screening"[All Fields] OR "Early Diagnosis of Cancer"[All Fields] OR "Cancer Early Diagnosis"[All Fields] #2 - ("algorithm s"[All Fields] OR "algorithmic"[All Fields] OR "algorithmically"[All Fields] OR "algorithmics"[All Fields] OR "algorithmization"[All Fields] OR "algorithms"[MeSH Terms] OR "algorithms"[All Fields] OR "algorithm"[All Fields] OR ("algorithm s"[All Fields] OR "algorithmic"[All Fields] OR "algorithmically"[All Fields] OR "algorithmics"[All Fields] OR "algorithmization"[All Fields] OR "algorithms"[MeSH Terms] OR "algorithms"[All Fields] OR "algorithm"[All Fields]) OR "intelligence artificial"[All Fields] OR "Computational Intelligence"[All Fields] OR "intelligence computational"[All Fields] OR "Machine Intelligence"[All Fields] OR "intelligence machine"[All Fields] OR "Computer Reasoning"[All Fields] OR "reasoning computer"[All Fields] OR "ai artificial intelligence"[All Fields] OR "computer assisted diagnosis cad"[All Fields] OR "CAD"[All Fields] OR "diagnosis computer assisted"[All Fields] OR "computer-assisted diagnosis"[All Fields] OR "computer assisted diagnosis"[All Fields] OR "Computer-Assisted Diagnoses"[All Fields] OR "diagnoses computer assisted"[All Fields] OR "Computer Vision Systems"[All Fields] OR "Computer Vision System"[All Fields] OR "system computer vision"[All Fields] OR "systems computer vision"[All Fields] OR ("Artificial Intelligence"[MeSH Terms] OR ("artificial"[All Fields] AND "intelligence"[All Fields]) OR "Artificial Intelligence"[All Fields] OR ("vision"[All Fields] AND "system"[All Fields] AND "Computer"[All Fields])) OR ("Artificial Intelligence"[MeSH Terms] OR ("artificial"[All Fields] AND "intelligence"[All Fields]) OR "Artificial Intelligence"[All Fields] OR ("vision"[All Fields] AND "systems"[All Fields] AND "Computer"[All Fields])) OR ("Artificial Intelligence"[MeSH Terms] OR ("artificial"[All Fields] AND "intelligence"[All Fields]) OR "Artificial Intelligence"[All Fields] OR ("knowledge"[All Fields] AND "acquisition"[All Fields] AND "Computer"[All Fields])) OR ("Artificial Intelligence"[MeSH Terms] OR ("artificial"[All Fields] AND "intelligence"[All Fields]) OR "Artificial Intelligence"[All Fields] OR ("acquisition"[All Fields] AND "knowledge"[All Fields] AND "Computer"[All Fields])) OR "knowledge representation computer"[All Fields] OR ("Artificial Intelligence"[MeSH Terms] OR ("artificial"[All Fields] AND "intelligence"[All Fields]) OR "Artificial Intelligence"[All Fields] OR ("knowledge"[All Fields] AND "representations"[All Fields] AND "Computer"[All Fields])) OR ("Artificial Intelligence"[MeSH Terms] OR ("artificial"[All Fields] AND "intelligence"[All Fields]) OR "Artificial Intelligence"[All Fields] OR ("representation"[All Fields] AND "knowledge"[All Fields] AND "Computer"[All Fields])) OR "Computer Neural Network"[All Fields] OR "Computer Neural Networks"[All Fields] OR ("neural networks, computer"[MeSH Terms] OR ("neural"[All Fields] AND "networks"[All Fields] AND "Computer"[All Fields]) OR "Computer Neural Networks"[All Fields] OR ("network"[All Fields] AND "Computer"[All Fields] AND "neural"[All Fields])) OR ("neural networks, computer"[MeSH Terms] OR ("neural"[All Fields] AND "networks"[All Fields] AND "Computer"[All Fields]) OR	227

(continued)

S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
	"Computer Neural Networks"[All Fields] OR ("networks"[All Fields] AND "Computer"[All Fields] AND "neural"[All Fields])) OR "neural network computer"[All Fields] OR "models neural network"[All Fields] OR "model neural network"[All Fields] OR "network model neural"[All Fields] OR ("neural networks, computer"[MeSH Terms] OR ("neural"[All Fields] AND "networks"[All Fields] AND "Computer"[All Fields]) OR "Computer Neural Networks"[All Fields] OR ("network"[All Fields] AND "models"[All Fields] AND "neural"[All Fields])) OR "Neural Network Model"[All Fields] OR "Neural Network Models"[All Fields] OR "Computational Neural Networks"[All Fields] OR "Computational Neural Network"[All Fields] OR ("neural networks, computer"[MeSH Terms] OR ("neural"[All Fields] AND "networks"[All Fields] AND "Computer"[All Fields]) OR "Computer Neural Networks"[All Fields] OR ("network"[All Fields] AND "computational"[All Fields] AND "neural"[All Fields])) OR "networks computational neural"[All Fields] OR "neural network computational"[All Fields] OR "neural networks computational"[All Fields] OR "artificial neural network"[All Fields] OR "convolutional neural network"[All Fields] OR "Deep Learning"[All Fields] OR "learning deep"[All Fields] OR "Hierarchical Learning"[All Fields] OR "learning hierarchical"[All Fields] OR "Machine Learning"[All Fields] OR "learning machine"[All Fields] OR "Transfer Learning"[All Fields] OR "learning transfer"[All Fields]) AND ("asynchronous service models"[All Fields] OR "remote technologies"[All Fields] OR "remote technology"[All Fields] OR "virtual platform"[All Fields] OR "virtual platforms"[All Fields] OR "Mobile-phone-based screening"[All Fields] OR "Mobile Applications"[All Fields] OR "application mobile"[All Fields] OR "applications mobile"[All Fields] OR "Mobile Application"[All Fields] OR "Mobile Apps"[All Fields] OR "app mobile"[All Fields] OR "apps mobile"[All Fields] OR "Mobile App"[All Fields] OR "Portable Electronic Apps"[All Fields] OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("app"[All Fields] AND "portable"[All Fields] AND "electronic"[All Fields])) OR (("appl plant sci"[Journal] OR "apps"[All Fields]) AND ("portability"[All Fields] OR "portable"[All Fields] OR "portables"[All Fields]) AND ("electronical"[All Fields] OR "electronically"[All Fields] OR "electronics"[MeSH Terms] OR "electronics"[All Fields] OR "electronic"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("electronic"[All Fields] AND "app"[All Fields] AND "portable"[All Fields])) OR (("electronical"[All Fields] OR "electronically"[All Fields] OR "electronics"[MeSH Terms] OR "electronics"[All Fields] OR "electronic"[All Fields]) AND ("appl plant sci"[Journal] OR "apps"[All Fields]) AND ("portability"[All Fields] OR "portable"[All Fields] OR "portables"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("portable"[All Fields] AND "electronic"[All Fields] AND "app"[All Fields])) OR "Portable Electronic Applications"[All Fields] OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("application"[All Fields] AND "portable"[All Fields] AND "electronic"[All Fields])) OR "applications portable electronic"[All Fields] OR "electronic application portable"[All Fields] OR (("electronical"[All Fields] OR "electronically"[All Fields] OR "electronics"[MeSH Terms] OR "electronics"[All Fields] OR "electronic"[All Fields]) AND ("applicabilities"[All Fields] OR "applicability"[All Fields] OR "application"[All Fields] OR "applications"[All Fields] OR "applicative"[All Fields]) AND ("portability"[All Fields] OR "portable"[All Fields] OR "portables"[All Fields])) OR "Portable Electronic Application"[All Fields] OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("portable"[All Fields] AND "software"[All Fields] AND "apps"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("app"[All Fields] AND "portable"[All Fields] AND "software"[All Fields])) OR (("appl plant sci"[Journal] OR "apps"[All Fields]) AND ("portability"[All Fields] OR "portable"[All Fields] OR "portables"[All Fields]) AND ("software"[MeSH Terms] OR "software"[All Fields] OR "software s"[All Fields] OR "softwares"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("portable"[All Fields] AND "software"[All Fields]	*(continued)*

S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
	AND "app"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("software"[All Fields] AND "app"[All Fields] AND "portable"[All Fields])) OR (("software"[MeSH Terms] OR "software"[All Fields] OR "software s"[All Fields] OR "softwares"[All Fields]) AND ("appl plant sci"[Journal] OR "apps"[All Fields]) AND ("portability"[All Fields] OR "portable"[All Fields] OR "portables"[All Fields])) OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("portable"[All Fields] AND "software"[All Fields] AND "applications"[All Fields])) OR "application portable software"[All Fields] OR (("applicabilities"[All Fields] OR "applicability"[All Fields] OR "application"[All Fields] OR "applications"[All Fields] OR "applicative"[All Fields]) AND ("portability"[All Fields] OR "portable"[All Fields] OR "portables"[All Fields]) AND ("software"[MeSH Terms] OR "software"[All Fields] OR "software s"[All Fields] OR "softwares"[All Fields])) OR "Portable Software Application"[All Fields] OR ("Mobile Applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "Mobile Applications"[All Fields] OR ("software"[All Fields] AND "application"[All Fields] AND "portable"[All Fields])) OR (("software"[MeSH Terms] OR "software"[All Fields] OR "software s"[All Fields] OR "softwares"[All Fields]) AND ("applicabilities"[All Fields] OR "applicability"[All Fields] OR "application"[All Fields] OR "applications"[All Fields] OR "applicative"[All Fields]) AND ("portability"[All Fields] OR "portable"[All Fields] OR "portables"[All Fields])) OR "Computer Software"[All Fields] OR "software computer"[All Fields] OR "Computer Programs"[All Fields] OR "Computer Program"[All Fields] OR "program computer"[All Fields] OR "programs computer"[All Fields] OR "Software Tools"[All Fields] OR "Software Tool"[All Fields] OR "tool software"[All Fields] OR "tools software"[All Fields] OR "Computer Applications Software"[All Fields] OR ("software"[MeSH Terms] OR "software"[All Fields] OR ("applications"[All Fields] AND "software"[All Fields] AND "Computer"[All Fields])) OR ("software"[MeSH Terms] OR "software"[All Fields] OR ("applications"[All Fields] AND "softwares"[All Fields] AND "Computer"[All Fields])) OR ("software"[MeSH Terms] OR "software"[All Fields] OR ("Computer"[All Fields] AND "applications"[All Fields] AND "softwares"[All Fields])) OR ("software"[MeSH Terms] OR "software"[All Fields] OR ("software"[All Fields] AND "Computer"[All Fields] AND "applications"[All Fields])) OR ("software"[MeSH Terms] OR "software"[All Fields] OR ("softwares"[All Fields] AND "Computer"[All Fields] AND "applications"[All Fields])) OR "Computer Software Applications"[All Fields] OR ("software"[MeSH Terms] OR "software"[All Fields] OR ("application"[All Fields] AND "Computer"[All Fields] AND "software"[All Fields])) OR "applications computer software"[All Fields] OR "Computer Software Application"[All Fields] OR "software application computer"[All Fields] OR "software applications computer"[All Fields] OR "applications medical informatics"[All Fields] OR ("medical informatics applications"[MeSH Terms] OR ("medical"[All Fields] AND "informatics"[All Fields] AND "applications"[All Fields]) OR "medical informatics applications"[All Fields] OR ("informatics"[All Fields] AND "applications"[All Fields] AND "medical"[All Fields])) OR ("medical informatics applications"[MeSH Terms] OR ("medical"[All Fields] AND "informatics"[All Fields] AND "applications"[All Fields]) OR "medical informatics applications"[All Fields] OR ("application"[All Fields] AND "medical"[All Fields] AND "informatics"[All Fields])) OR ("medical informatics applications"[MeSH Terms] OR ("medical"[All Fields] AND "informatics"[All Fields] AND "applications"[All Fields]) OR "medical informatics applications"[All Fields] OR ("informatics"[All Fields] AND "application"[All Fields] AND "medical"[All Fields])) OR "Medical Informatics Application"[All Fields] OR "Computer Programs and Programming"[All Fields] OR "Software Engineering"[All Fields] OR "engineering software"[All Fields] OR "virtual consultation"[All Fields] OR "virtual consultations"[All Fields] OR (("virtual"[All Fields] OR "virtuality"[All Fields] OR "virtualization"[All Fields] OR "virtualized"[All Fields] OR "virtualizing"[All Fields] OR "virtuals"[All Fields]) AND "online"[All Fields] AND ("consultancies"[All Fields] OR "consultancy"[All Fields] OR "consultant s"[All Fields] OR "consultants"[MeSH Terms] OR "consultants"[All Fields] OR "consultant"[All Fields] OR "consultative"[All Fields] OR "consulter"[All Fields] OR "consulters"[All Fields] OR "referral and consultation"[MeSH Terms] OR ("referral"[All Fields] AND	*(continued)*

S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
	"consultation"[All Fields]) OR "referral and consultation"[All Fields] OR "consult"[All Fields] OR "consultation"[All Fields] OR "consultations"[All Fields] OR "consulted"[All Fields] OR "consulting"[All Fields] OR "consults"[All Fields])) OR (("virtual"[All Fields] OR "virtuality"[All Fields] OR "virtualization"[All Fields] OR "virtualized"[All Fields] OR "virtualizing"[All Fields] OR "virtuals"[All Fields]) AND "online"[All Fields] AND ("consultancies"[All Fields] OR "consultancy"[All Fields] OR "consultant s"[All Fields] OR "consultants"[MeSH Terms] OR "consultants"[All Fields] OR "consultant"[All Fields] OR "consultative"[All Fields] OR "consulter"[All Fields] OR "consulters"[All Fields] OR "referral and consultation"[MeSH Terms] OR ("referral"[All Fields] AND "consultation"[All Fields]) OR "referral and consultation"[All Fields] OR "consult"[All Fields] OR "consultation"[All Fields] OR "consultations"[All Fields] OR "consulted"[All Fields] OR "consulting"[All Fields] OR "consults"[All Fields])) OR "Virtual Care"[All Fields] OR "E-consultation"[All Fields] OR "e-referral"[All Fields] OR "remote consultation"[All Fields] OR "tele-consultation"[All Fields] OR "video-consultation"[All Fields])	
	#3 - "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "neoplasia"[All Fields] OR "neoplasias"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "neoplasia"[All Fields] OR "neoplasias"[All Fields] OR "neoplasm s"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "neoplasm"[All Fields] OR "cysts"[MeSH Terms] OR "cysts"[All Fields] OR "cyst"[All Fields] OR "neurofibroma"[MeSH Terms] OR "neurofibroma"[All Fields] OR "neurofibromas"[All Fields] OR "tumor s"[All Fields] OR "tumoral"[All Fields] OR "tumorous"[All Fields] OR "tumour"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "tumor"[All Fields] OR "tumour s"[All Fields] OR "tumoural"[All Fields] OR "tumourous"[All Fields] OR "tumours"[All Fields] OR "tumors"[All Fields] OR "cysts"[MeSH Terms] OR "cysts"[All Fields] OR "cyst"[All Fields] OR "neurofibroma"[MeSH Terms] OR "neurofibroma"[All Fields] OR "neurofibromas"[All Fields] OR "tumor s"[All Fields] OR "tumoral"[All Fields] OR "tumorous"[All Fields] OR "tumour"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "tumor"[All Fields] OR "tumour s"[All Fields] OR "tumoural"[All Fields] OR "tumourous"[All Fields] OR "tumours"[All Fields] OR "tumors"[All Fields] OR "cancer s"[All Fields] OR "cancerated"[All Fields] OR "canceration"[All Fields] OR "cancerization"[All Fields] OR "cancerized"[All Fields] OR "cancerous"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields] OR "cancers"[All Fields] OR "cancer s"[All Fields] OR "cancerated"[All Fields] OR "canceration"[All Fields] OR "cancerization"[All Fields] OR "cancerized"[All Fields] OR "cancerous"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields] OR "cancers"[All Fields] OR "malign"[All Fields] OR "malignance"[All Fields] OR "malignances"[All Fields] OR "malignant"[All Fields] OR "malignants"[All Fields] OR "malignities"[All Fields] OR "malignity"[All Fields] OR "malignization"[All Fields] OR "malignized"[All Fields] OR "maligns"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "malignancies"[All Fields] OR "malignancy"[All Fields] OR "malign"[All Fields] OR "malignance"[All Fields] OR "malignances"[All Fields] OR "malignant"[All Fields] OR "malignants"[All Fields] OR "malignities"[All Fields] OR "malignity"[All Fields] OR "malignization"[All Fields] OR "malignized"[All Fields] OR "maligns"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "malignancies"[All Fields] OR "malignancy"[All Fields] OR "Malignant Neoplasms"[All Fields] OR "Malignant Neoplasm"[All Fields] OR "neoplasm malignant"[All Fields] OR "neoplasms malignant"[All Fields] OR "Benign Neoplasms"[All Fields] OR "neoplasms benign"[All Fields] OR "Benign Neoplasm"[All Fields] OR "neoplasm benign"[All Fields]	
	#4 - "Systematic Review"[All Fields] OR "meta analysis"[All Fields] OR "Metanalysis"[All Fields] OR "meta analysis"[All Fields]	
	#5 - #1 AND #2 AND #3 AND #4	

(continued)

S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
Cochrane Library	#1 - diagnoses OR diagnose OR "Diagnoses and Examinations" OR "Examinations and Diagnoses" OR "Postmortem Diagnosis" OR "Diagnoses, Postmortem" OR "Diagnosis, Postmortem" OR "Postmortem Diagnoses" OR "Antemortem Diagnosis" OR "Antemortem Diagnoses" OR "Diagnoses, Antemortem" OR "Diagnosis, Antemortem" OR "Oral cancer diagnosis" OR "computer-aided diagnosis" OR " Cancer Early Detection" OR "Cancer Screening" OR "Screening, Cancer" OR "non-invasive screening" OR "Cancer Screening Tests" OR "Cancer Screening Test" OR "Screening Test, Cancer" OR "Screening Tests, Cancer" OR "Test, Cancer Screening" OR "Tests, Cancer Screening" OR "Early Diagnosis of Cancer" OR "Cancer Early Diagnosis" #2 - ((Algorithm OR Algorithms OR "Intelligence, Artificial" OR "Computational Intelligence" OR "Intelligence, Computational" OR "Machine Intelligence" OR "Intelligence, Machine" OR "Computer Reasoning" OR "Reasoning, Computer" OR "AI (Artificial Intelligence)" OR “computer-assisted diagnosis (CAD)” OR “(CAD)” OR “Diagnosis, Computer Assisted” OR “Computer-Assisted Diagnosis” OR “Computer Assisted Diagnosis” OR “Computer-Assisted Diagnoses” OR “Diagnoses, Computer-Assisted” OR "Computer Vision Systems" OR "Computer Vision System" OR "System, Computer Vision" OR "Systems, Computer Vision" OR "Vision System, Computer" OR "Vision Systems, Computer" OR "Knowledge Acquisition (Computer)" OR "Acquisition, Knowledge (Computer)" OR "Knowledge Representation (Computer)" OR "Knowledge Representations (Computer)" OR "Representation, Knowledge (Computer)" OR "Computer Neural Network" OR "Computer Neural Networks" OR "Network, Computer Neural" OR "Networks, Computer Neural" OR "Neural Network, Computer" OR "Models, Neural Network" OR "Model, Neural Network" OR "Network Model, Neural" OR "Network Models, Neural" OR "Neural Network Model" OR "Neural Network Models" OR "Computational Neural Networks" OR "Computational Neural Network" OR "Network, Computational Neural" OR "Networks, Computational Neural" OR "Neural Network, Computational" OR "Neural Networks, Computational" OR "artificial neural network" OR "convolutional neural network" OR "Deep Learning" OR "Learning, Deep" OR "Hierarchical Learning" OR "Learning, Hierarchical" OR "Machine Learning" OR "Learning, Machine" OR "Transfer Learning" OR "Learning, Transfer") AND ("asynchronous service models" OR "remote technologies" OR "remote technology" OR "virtual platform" OR "virtual platforms" OR "Mobile-phone-based screening" OR "Mobile Applications" OR "Application, Mobile" OR "Applications, Mobile" OR "Mobile Application" OR "Mobile Apps" OR "App, Mobile" OR "Apps, Mobile" OR "Mobile App" OR "Portable Electronic Apps" OR "App, Portable Electronic" OR "Apps, Portable Electronic" OR "Electronic App, Portable" OR "Electronic Apps, Portable" OR "Portable Electronic App" OR "Portable Electronic Applications" OR "Application, Portable Electronic" OR "Applications, Portable Electronic" OR "Electronic Application, Portable" OR "Electronic Applications, Portable" OR "Portable Electronic Application" OR "Portable Software Apps" OR "App, Portable Software" OR "Apps, Portable Software" OR "Portable Software App" OR "Software App, Portable" OR "Software Apps, Portable" OR "Portable Software Applications" OR "Application, Portable Software" OR "Applications, Portable Software" OR "Portable Software Application" OR "Software Application, Portable" OR "Software Applications, Portable" OR "Computer Software" OR "Software, Computer" OR "Computer Programs" OR "Computer Program" OR "Program, Computer" OR "Programs, Computer" OR "Software Tools" OR "Software Tool" OR "Tool, Software" OR "Tools, Software" OR "Computer Applications Software" OR "Applications Software, Computer" OR "Applications Softwares, Computer" OR "Computer Applications Softwares" OR "Software, Computer Applications" OR "Softwares, Computer Applications" OR "Computer Software Applications" OR "Application, Computer Software" OR "Applications, Computer Software" OR "Computer Software Application" OR "Software Application, Computer" OR "Software Applications, Computer" OR "Applications, Medical Informatics" OR "Informatics Applications, Medical" OR "Application, Medical Informatics" OR "Informatics Application, Medical" OR "Medical Informatics Application" OR "Computer Programs and Programming" OR "Software Engineering" OR "Engineering, Software" OR "virtual consultation" OR "virtual consultations" OR	57 *(continued)*

S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
	"Virtual online consultation" OR "Virtual online consultations" OR "Virtual Care" OR "E-consultation" OR "e-referral" OR "remote consultation" OR tele-consultation OR "video-consultation"))	
	#3 - Neoplasia OR Neoplasias OR Neoplasm OR Tumors OR Tumor OR Cancer OR Cancers OR Malignancy OR Malignancies OR "Malignant Neoplasms" OR "Malignant Neoplasm" OR "Neoplasm, Malignant" OR "Neoplasms, Malignant" OR "Benign Neoplasms" OR "Neoplasms, Benign" OR "Benign Neoplasm" OR "Neoplasm, Benign"	
	#4 "Systematic Review" OR "Meta-analysis" OR "Metanalysis" OR "Meta analysis"	
	#5 #1 AND #2 AND #3 AND #4	
Scopus	TITLE-ABS-KEY (diagnoses OR diagnose OR "Diagnoses and Examinations" OR "Examinations and Diagnoses" OR "Postmortem Diagnosis" OR "Diagnoses, Postmortem" OR "Diagnosis, Postmortem" OR "Postmortem Diagnoses" OR "Antemortem Diagnosis" OR "Antemortem Diagnoses" OR "Diagnoses, Antemortem" OR "Diagnosis, Antemortem" OR "Oral cancer diagnosis" OR "computer-aided diagnosis" OR " Cancer Early Detection" OR "Cancer Screening" OR "Screening, Cancer" OR "non-invasive screening" OR "Cancer Screening Tests" OR "Cancer Screening Test" OR "Screening Test, Cancer" OR "Screening Tests, Cancer" OR "Test, Cancer Screening" OR "Tests, Cancer Screening" OR "Early Diagnosis of Cancer" OR "Cancer Early Diagnosis") AND TITLE-ABS-KEY ((algorithm OR algorithms OR "Intelligence, Artificial" OR "Computational Intelligence" OR "Intelligence, Computational" OR "Machine Intelligence" OR "Intelligence, Machine" OR "Computer Reasoning" OR "Reasoning, Computer" OR "AI (Artificial Intelligence)" OR "computer-assisted diagnosis (CAD)" OR "(CAD)" OR "Diagnosis, Computer Assisted" OR "Computer-Assisted Diagnosis" OR "Computer Assisted Diagnosis" OR "Computer-Assisted Diagnoses" OR "Diagnoses, Computer-Assisted" OR "Computer Vision Systems" OR "Computer Vision System" OR "System, Computer Vision" OR "Systems, Computer Vision" OR "Vision System, Computer" OR "Vision Systems, Computer" OR "Knowledge Acquisition (Computer)" OR "Acquisition, Knowledge (Computer)" OR "Knowledge Representation (Computer)" OR "Knowledge Representations (Computer)" OR "Representation, Knowledge (Computer)" OR "Computer Neural Network" OR "Computer Neural Networks" OR "Network, Computer Neural" OR "Networks, Computer Neural" OR "Neural Network, Computer" OR "Models, Neural Network" OR "Model, Neural Network" OR "Network Model, Neural" OR "Network Models, Neural" OR "Neural Network Model" OR "Neural Network Models" OR "Computational Neural Networks" OR "Computational Neural Network" OR "Network, Computational Neural" OR "Networks, Computational Neural" OR "Neural Network, Computational" OR "Neural Networks, Computational" OR "artificial neural network" OR "convolutional neural network" OR "Deep Learning" OR "Learning, Deep" OR "Hierarchical Learning" OR "Learning, Hierarchical" OR "Machine Learning" OR "Learning, Machine" OR "Transfer Learning" OR "Learning, Transfer") AND ("asynchronous service models" OR "remote technologies" OR "remote technology" OR "virtual platform" OR "virtual platforms" OR "Mobile-phone-based screening" OR "Mobile Applications" OR "Application, Mobile" OR "Applications, Mobile" OR "Mobile Application" OR "Mobile Apps" OR "App, Mobile" OR "Apps, Mobile" OR "Mobile App" OR "Portable Electronic Apps" OR "App, Portable Electronic" OR "Apps, Portable Electronic" OR "Electronic App, Portable" OR "Electronic Apps, Portable" OR "Portable Electronic App" OR "Portable Electronic Applications" OR "Application, Portable Electronic" OR "Applications, Portable Electronic" OR "Electronic Application, Portable" OR "Electronic Applications, Portable" OR "Portable Electronic Application" OR "Portable Software Apps" OR "App, Portable Software" OR "Apps, Portable Software" OR "Portable Software App" OR "Software App, Portable" OR "Software Apps, Portable" OR "Portable Software Applications" OR "Application, Portable Software" OR "Applications, Portable Software" OR "Portable Software Application" OR "Software Application, Portable" OR "Software Applications, Portable" OR "Computer Software" OR "Software, Computer" OR "Computer Programs" OR "Computer Program" OR "Program, Computer" OR "Programs, Computer" OR	22

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S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
	"Software Tools" OR "Software Tool" OR "Tool, Software" OR "Tools, Software" OR "Computer Applications Software" OR "Applications Software, Computer" OR "Applications Softwares, Computer" OR "Computer Applications Softwares" OR "Software, Computer Applications" OR "Softwares, Computer Applications" OR "Computer Software Applications" OR "Application, Computer Software" OR "Applications, Computer Software" OR "Computer Software Application" OR "Software Application, Computer" OR "Software Applications, Computer" OR "Applications, Medical Informatics" OR "Informatics Applications, Medical" OR "Application, Medical Informatics" OR "Informatics Application, Medical" OR "Medical Informatics Application" OR "Computer Programs and Programming" OR "Software Engineering" OR "Engineering, Software" OR "virtual consultation" OR "virtual consultations" OR "Virtual online consultation" OR "Virtual online consultations" OR "Virtual Care" OR "E-consultation" OR "e-referral" OR "remote consultation" OR tele-consultation OR "video-consultation")) TITLE-ABS-KEY (neoplasia OR neoplasias OR neoplasm OR tumors OR tumor OR cancer OR cancers OR malignancy OR malignancies OR "Malignant Neoplasms" OR "Malignant Neoplasm" OR "Neoplasm, Malignant" OR "Neoplasms, Malignant" OR "Benign Neoplasms" OR "Neoplasms, Benign" OR "Benign Neoplasm" OR "Neoplasm, Benign") AND TITLE-ABS-KEY ("Systematic Review" OR "Meta-analysis" OR "Metanalysis" OR "Meta analysis")	
Web of Science	#1- TS=(Diagnoses OR Diagnose OR "Diagnoses and Examinations" OR "Examinations and Diagnoses" OR "Postmortem Diagnosis" OR "Diagnoses, Postmortem" OR "Diagnosis, Postmortem" OR "Postmortem Diagnoses" OR "Antemortem Diagnosis" OR "Antemortem Diagnoses" OR "Diagnoses, Antemortem" OR "Diagnosis, Antemortem" OR "Oral cancer diagnosis" OR "computer-aided diagnosis" OR" Cancer Early Detection" OR "Cancer Screening" OR "Screening, Cancer" OR "non-invasive screening" OR "Cancer Screening Tests" OR "Cancer Screening Test" OR "Screening Test, Cancer" OR "Screening Tests, Cancer" OR "Test, Cancer Screening" OR "Tests, Cancer Screening" OR "Early Diagnosis of Cancer" OR "Cancer Early Diagnosis") #2- TS=((Algorithm OR Algorithms OR "Intelligence, Artificial" OR "Computational Intelligence" OR "Intelligence, Computational" OR "Machine Intelligence" OR "Intelligence, Machine" OR "Computer Reasoning" OR "Reasoning, Computer" OR "AI (Artificial Intelligence)" OR “computer-assisted diagnosis (CAD)” OR “(CAD)” OR “Diagnosis, Computer Assisted” OR “Computer-Assisted Diagnosis” OR “Computer Assisted Diagnosis” OR “Computer-Assisted Diagnoses” OR “Diagnoses, Computer-Assisted” OR "Computer Vision Systems" OR "Computer Vision System" OR "System, Computer Vision" OR "Systems, Computer Vision" OR "Vision System, Computer" OR "Vision Systems, Computer" OR "Knowledge Acquisition (Computer)" OR "Acquisition, Knowledge (Computer)" OR "Knowledge Representation (Computer)" OR "Knowledge Representations (Computer)" OR "Representation, Knowledge (Computer)" OR "Computer Neural Network" OR "Computer Neural Networks" OR "Network, Computer Neural" OR "Networks, Computer Neural" OR "Neural Network, Computer" OR "Models, Neural Network" OR "Model, Neural Network" OR "Network Model, Neural" OR "Network Models, Neural" OR "Neural Network Model" OR "Neural Network Models" OR "Computational Neural Networks" OR "Computational Neural Network" OR "Network, Computational Neural" OR "Networks, Computational Neural" OR "Neural Network, Computational" OR "Neural Networks, Computational" OR "artificial neural network" OR "convolutional neural network" OR "Deep Learning" OR "Learning, Deep" OR "Hierarchical Learning" OR "Learning, Hierarchical" OR "Machine Learning" OR "Learning, Machine" OR "Transfer Learning" OR "Learning, Transfer") AND ("asynchronous service models" OR "remote technologies" OR "remote technology" OR "virtual platform" OR "virtual platforms" OR "Mobile-phone-based screening" OR "Mobile Applications" OR "Application, Mobile" OR "Applications, Mobile" OR "Mobile Application" OR "Mobile Apps" OR "App, Mobile" OR "Apps, Mobile" OR "Mobile App" OR "Portable Electronic Apps" OR "App, Portable Electronic" OR "Apps, Portable Electronic" OR "Electronic App, Portable" OR "Electronic Apps, Portable" OR "Portable Electronic App" OR "Portable Electronic Applications" OR "Application, Portable Electronic" OR "Applications, Portable Electronic" OR "Electronic Application,	1

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S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
	Portable" OR "Electronic Applications, Portable" OR "Portable Electronic Application" OR "Portable Software Apps" OR "App, Portable Software" OR "Apps, Portable Software" OR "Portable Software App" OR "Software App, Portable" OR "Software Apps, Portable" OR "Portable Software Applications" OR "Application, Portable Software" OR "Applications, Portable Software" OR "Portable Software Application" OR "Software Application, Portable" OR "Software Applications, Portable" OR "Computer Software" OR "Software, Computer" OR "Computer Programs" OR "Computer Program" OR "Program, Computer" OR "Programs, Computer" OR "Software Tools" OR "Software Tool" OR "Tool, Software" OR "Tools, Software" OR "Computer Applications Software" OR "Applications Software, Computer" OR "Applications Softwares, Computer" OR "Computer Applications Softwares" OR "Software, Computer Applications" OR "Softwares, Computer Applications" OR "Computer Software Applications" OR "Application, Computer Software" OR "Applications, Computer Software" OR "Computer Software Application" OR "Software Application, Computer" OR "Software Applications, Computer" OR "Applications, Medical Informatics" OR "Informatics Applications, Medical" OR "Application, Medical Informatics" OR "Informatics Application, Medical" OR "Medical Informatics Application" OR "Computer Programs and Programming" OR "Software Engineering" OR "Engineering, Software" OR "virtual consultation" OR "virtual consultations" OR "Virtual online consultation" OR "Virtual online consultations" OR "Virtual Care" OR "E-consultation" OR "e-referral" OR "remote consultation" OR tele-consultation OR "video-consultation")) #3– TS=(Neoplasia OR Neoplasias OR Neoplasm OR Tumors OR Tumor OR Cancer OR Cancers OR Malignancy OR Malignancies OR "Malignant Neoplasms" OR "Malignant Neoplasm" OR "Neoplasm, Malignant" OR "Neoplasms, Malignant" OR "Benign Neoplasms" OR "Neoplasms, Benign" OR "Benign Neoplasm" OR "Neoplasm, Benign") #4 - TS=("Systematic Review" OR "Meta-analysis" OR "Metanalysis" OR "Meta analysis") #5 - #4 AND #3 AND #2 AND #1	
LILACS (via VHL Regional Portal)	(Diagnoses OR Diagnose OR "Diagnoses and Examinations" OR "Examinations and Diagnoses" OR "Postmortem Diagnosis" OR "Diagnoses, Postmortem" OR "Diagnosis, Postmortem" OR "Postmortem Diagnoses" OR "Antemortem Diagnosis" OR "Antemortem Diagnoses" OR "Diagnoses, Antemortem" OR "Diagnosis, Antemortem" OR "Oral cancer diagnosis" OR "computer-aided diagnosis" OR" Cancer Early Detection" OR "Cancer Screening" OR "Screening, Cancer" OR "non-invasive screening" OR "Cancer Screening Tests" OR "Cancer Screening Test" OR "Screening Test, Cancer" OR "Screening Tests, Cancer" OR "Test, Cancer Screening" OR "Tests, Cancer Screening" OR "Early Diagnosis of Cancer" OR "Cancer Early Diagnosis") AND (((Algorithm OR Algorithms OR "Intelligence, Artificial" OR "Computational Intelligence" OR "Intelligence, Computational" OR "Machine Intelligence" OR "Intelligence, Machine" OR "Computer Reasoning" OR "Reasoning, Computer" OR "AI (Artificial Intelligence)" OR “computer-assisted diagnosis (CAD)” OR “(CAD)” OR “Diagnosis, Computer Assisted” OR “Computer-Assisted Diagnosis” OR “Computer Assisted Diagnosis” OR “Computer-Assisted Diagnoses” OR “Diagnoses, Computer-Assisted” OR "Computer Vision Systems" OR "Computer Vision System" OR "System, Computer Vision" OR "Systems, Computer Vision" OR "Vision System, Computer" OR "Vision Systems, Computer" OR "Knowledge Acquisition (Computer)" OR "Acquisition, Knowledge (Computer)" OR "Knowledge Representation (Computer)" OR "Knowledge Representations (Computer)" OR "Representation, Knowledge (Computer)" OR "Computer Neural Network" OR "Computer Neural Networks" OR "Network, Computer Neural" OR "Networks, Computer Neural" OR "Neural Network, Computer" OR "Models, Neural Network" OR "Model, Neural Network" OR "Network Model, Neural" OR "Network Models, Neural" OR "Neural Network Model" OR "Neural Network Models" OR "Computational Neural Networks" OR "Computational Neural Network" OR "Network, Computational Neural" OR "Networks, Computational Neural" OR "Neural Network, Computational" OR "Neural Networks, Computational" OR "artificial neural network" OR "convolutional neural network" OR "Deep Learning" OR "Learning,	0

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S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
	Deep" OR "Hierarchical Learning" OR "Learning, Hierarchical" OR "Machine Learning" OR "Learning, Machine" OR "Transfer Learning" OR "Learning, Transfer") AND ("asynchronous service models" OR "remote technologies" OR "remote technology" OR "virtual platform" OR "virtual platforms" OR "Mobile-phone-based screening" OR "Mobile Applications" OR "Application, Mobile" OR "Applications, Mobile" OR "Mobile Application" OR "Mobile Apps" OR "App, Mobile" OR "Apps, Mobile" OR "Mobile App" OR "Portable Electronic Apps" OR "App, Portable Electronic" OR "Apps, Portable Electronic" OR "Electronic App, Portable" OR "Electronic Apps, Portable" OR "Portable Electronic App" OR "Portable Electronic Applications" OR "Application, Portable Electronic" OR "Applications, Portable Electronic" OR "Electronic Application, Portable" OR "Electronic Applications, Portable" OR "Portable Electronic Application" OR "Portable Software Apps" OR "App, Portable Software" OR "Apps, Portable Software" OR "Portable Software App" OR "Software App, Portable" OR "Software Apps, Portable" OR "Portable Software Applications" OR "Application, Portable Software" OR "Applications, Portable Software" OR "Portable Software Application" OR "Software Application, Portable" OR "Software Applications, Portable" OR "Computer Software" OR "Software, Computer" OR "Computer Programs" OR "Computer Program" OR "Program, Computer" OR "Programs, Computer" OR "Software Tools" OR "Software Tool" OR "Tool, Software" OR "Tools, Software" OR "Computer Applications Software" OR "Applications Software, Computer" OR "Applications Softwares, Computer" OR "Computer Applications Softwares" OR "Software, Computer Applications" OR "Softwares, Computer Applications" OR "Computer Software Applications" OR "Application, Computer Software" OR "Applications, Computer Software" OR "Computer Software Application" OR "Software Application, Computer" OR "Software Applications, Computer" OR "Applications, Medical Informatics" OR "Informatics Applications, Medical" OR "Application, Medical Informatics" OR "Informatics Application, Medical" OR "Medical Informatics Application" OR "Computer Programs and Programming" OR "Software Engineering" OR "Engineering, Software" OR "virtual consultation" OR "virtual consultations" OR "Virtual online consultation" OR "Virtual online consultations" OR "Virtual Care" OR "E-consultation" OR "e-referral" OR "remote consultation" OR tele-consultation OR "video-consultation"))) AND (Neoplasia OR Neoplasias OR Neoplasm OR Tumors OR Tumor OR Cancer OR Cancers OR Malignancy OR Malignancies OR "Malignant Neoplasms" OR "Malignant Neoplasm" OR "Neoplasm, Malignant" OR "Neoplasms, Malignant" OR "Benign Neoplasms" OR "Neoplasms, Benign" OR "Benign Neoplasm" OR "Neoplasm, Benign") AND ("Systematic Review" OR "Meta-analysis" OR "Metanalysis" OR "Meta analysis")	
EMBASE	((diagnoses OR diagnose OR 'diagnoses and examinations' OR 'examinations and diagnoses'/exp OR 'examinations and diagnoses' OR 'postmortem diagnosis' OR 'diagnoses, postmortem' OR 'diagnosis, postmortem' OR 'postmortem diagnoses' OR 'antemortem diagnosis' OR 'antemortem diagnoses' OR 'diagnoses, antemortem' OR 'diagnosis, antemortem' OR 'oral cancer diagnosis' OR 'computer-aided diagnosis' OR 'cancer early detection' OR 'cancer screening'/exp OR 'cancer screening' OR 'screening, cancer'/exp OR 'screening, cancer' OR 'non-invasive screening' OR 'cancer screening tests' OR 'cancer screening test' OR 'screening test, cancer' OR 'screening tests, cancer' OR 'test, cancer screening' OR 'tests, cancer screening' OR 'early diagnosis of cancer' OR 'cancer early diagnosis') AND ('algorithm'/exp OR algorithm OR 'algorithms'/exp OR algorithms OR 'intelligence, artificial' OR 'computational intelligence'/exp OR 'computational intelligence' OR 'intelligence, computational' OR 'machine intelligence'/exp OR 'machine intelligence' OR 'intelligence, machine' OR 'computer reasoning'/exp OR 'computer reasoning' OR 'reasoning, computer' OR 'ai (artificial intelligence)' OR 'computer-assisted diagnosis (cad)' OR '(cad)' OR 'diagnosis, computer assisted'/exp OR 'diagnosis, computer assisted' OR 'computer-assisted diagnosis'/exp OR 'computer-assisted diagnosis' OR 'computer assisted diagnosis'/exp OR 'computer assisted diagnosis' OR 'computer-assisted diagnoses' OR 'diagnoses, computer-assisted' OR 'computer vision systems' OR 'computer vision system' OR 'system, computer vision' OR 'systems, computer vision' OR 'vision	30

(continued)

S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
	system, computer' OR 'vision systems, computer' OR 'knowledge acquisition (computer)' OR 'acquisition, knowledge (computer)' OR 'knowledge representation (computer)' OR 'knowledge representations (computer)' OR 'representation, knowledge (computer)' OR 'computer neural network'/exp OR 'computer neural network' OR 'computer neural networks'/exp OR 'computer neural networks' OR 'network, computer neural' OR 'networks, computer neural' OR 'neural network, computer'/exp OR 'neural network, computer' OR 'models, neural network' OR 'model, neural network' OR 'network model, neural' OR 'network models, neural' OR 'neural network model'/exp OR 'neural network model' OR 'neural network models' OR 'computational neural networks' OR 'computational neural network'/exp OR 'computational neural network' OR 'network, computational neural' OR 'networks, computational neural' OR 'neural network, computational' OR 'neural networks, computational' OR 'artificial neural network'/exp OR 'artificial neural network' OR 'convolutional neural network'/exp OR 'convolutional neural network' OR 'deep learning'/exp OR 'deep learning' OR 'learning, deep' OR 'hierarchical learning'/exp OR 'hierarchical learning' OR 'learning, hierarchical' OR 'machine learning'/exp OR 'machine learning' OR 'learning, machine'/exp OR 'learning, machine' OR 'transfer learning'/exp OR 'transfer learning' OR 'learning, transfer'/exp OR 'learning, transfer') AND ('asynchronous service models' OR 'remote technologies' OR 'remote technology' OR 'virtual platform' OR 'virtual platforms' OR 'mobile-phone-based screening' OR 'mobile applications'/exp OR 'mobile applications' OR 'application, mobile' OR 'applications, mobile' OR 'mobile application'/exp OR 'mobile application' OR 'mobile apps'/exp OR 'mobile apps' OR 'app, mobile' OR 'apps, mobile' OR 'mobile app'/exp OR 'mobile app' OR 'portable electronic apps' OR 'app, portable electronic' OR 'apps, portable electronic' OR 'electronic app, portable' OR 'electronic apps, portable' OR 'portable electronic app' OR 'portable electronic applications' OR 'application, portable electronic' OR 'applications, portable electronic' OR 'electronic application, portable' OR 'electronic applications, portable' OR 'portable electronic application' OR 'portable software apps'/exp OR 'portable software apps' OR 'app, portable software' OR 'apps, portable software' OR 'portable software app'/exp OR 'portable software app' OR 'software app, portable' OR 'software apps, portable' OR 'portable software applications'/exp OR 'portable software applications' OR 'application, portable software' OR 'applications, portable software' OR 'portable software application'/exp OR 'portable software application' OR 'software application, portable' OR 'software applications, portable' OR 'computer software' OR 'software, computer' OR 'computer programs' OR 'computer program'/exp OR 'computer program' OR 'program, computer'/exp OR 'program, computer' OR 'programs, computer' OR 'software tools' OR 'software tool' OR 'tool, software' OR 'tools, software' OR 'computer applications software' OR 'applications software, computer' OR 'applications softwares, computer' OR 'computer applications softwares' OR 'software, computer applications' OR 'softwares, computer applications' OR 'computer software applications' OR 'application, computer software' OR 'applications, computer software' OR 'computer software application' OR 'software application, computer' OR 'software applications, computer' OR 'applications, medical informatics' OR 'informatics applications, medical' OR 'application, medical informatics' OR 'informatics application, medical' OR 'medical informatics application' OR 'computer programs and programming'/exp OR 'computer programs and programming' OR 'software engineering' OR 'engineering, software' OR 'virtual consultation' OR 'virtual consultations' OR 'virtual online consultation' OR 'virtual online consultations' OR 'virtual care'/exp OR 'virtual care' OR 'e-consultation'/exp OR 'e-consultation' OR 'e-referral' OR 'remote consultation'/exp OR 'remote consultation' OR 'tele consultation'/exp OR 'tele consultation' OR 'video-consultation'/exp OR 'video-consultation') AND ('neoplasia'/exp OR neoplasia OR neoplasias OR 'neoplasm'/exp OR neoplasm OR 'tumors'/exp OR tumors OR 'tumor'/exp OR tumor OR 'cancer'/exp OR cancer OR 'cancers'/exp OR cancers OR 'malignancy'/exp OR malignancy OR 'malignancies'/exp	*(continued)*

S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
	OR malignancies OR 'malignant neoplasms' OR 'malignant neoplasm'/exp OR 'malignant neoplasm' OR 'neoplasm, malignant' OR 'neoplasms, malignant' OR 'benign neoplasms' OR 'neoplasms, benign' OR 'benign neoplasm'/exp OR 'benign neoplasm' OR 'neoplasm, benign'/exp OR 'neoplasm, benign') AND ('systematic review'/exp OR 'systematic review' OR 'meta-analysis'/exp OR 'meta-analysis' OR 'metanalysis' OR 'meta analysis'/exp OR 'meta analysis')	
EBSCOhost (All databases)	(diagnoses OR diagnose OR "Diagnoses and Examinations" OR "Examinations and Diagnoses" OR "Postmortem Diagnosis" OR "Diagnoses, Postmortem" OR "Diagnosis, Postmortem" OR "Postmortem Diagnoses" OR "Antemortem Diagnosis" OR "Antemortem Diagnoses" OR "Diagnoses, Antemortem" OR "Diagnosis, Antemortem" OR "Oral cancer diagnosis" OR "computer-aided diagnosis" OR " Cancer Early Detection" OR "Cancer Screening" OR "Screening, Cancer" OR "non-invasive screening" OR "Cancer Screening Tests" OR "Cancer Screening Test" OR "Screening Test, Cancer" OR "Screening Tests, Cancer" OR "Test, Cancer Screening" OR "Tests, Cancer Screening" OR "Early Diagnosis of Cancer" OR "Cancer Early Diagnosis") AND (((Algorithm OR Algorithms OR "Intelligence, Artificial" OR "Computational Intelligence" OR "Intelligence, Computational" OR "Machine Intelligence" OR "Intelligence, Machine" OR "Computer Reasoning" OR "Reasoning, Computer" OR "AI (Artificial Intelligence)" OR “computer-assisted diagnosis (CAD)” OR “(CAD)” OR “Diagnosis, Computer Assisted” OR “Computer-Assisted Diagnosis” OR “Computer Assisted Diagnosis” OR “Computer-Assisted Diagnoses” OR “Diagnoses, Computer-Assisted” OR "Computer Vision Systems" OR "Computer Vision System" OR "System, Computer Vision" OR "Systems, Computer Vision" OR "Vision System, Computer" OR "Vision Systems, Computer" OR "Knowledge Acquisition (Computer)" OR "Acquisition, Knowledge (Computer)" OR "Knowledge Representation (Computer)" OR "Knowledge Representations (Computer)" OR "Representation, Knowledge (Computer)" OR "Computer Neural Network" OR "Computer Neural Networks" OR "Network, Computer Neural" OR "Networks, Computer Neural" OR "Neural Network, Computer" OR "Models, Neural Network" OR "Model, Neural Network" OR "Network Model, Neural" OR "Network Models, Neural" OR "Neural Network Model" OR "Neural Network Models" OR "Computational Neural Networks" OR "Computational Neural Network" OR "Network, Computational Neural" OR "Networks, Computational Neural" OR "Neural Network, Computational" OR "Neural Networks, Computational" OR "artificial neural network" OR "convolutional neural network" OR "Deep Learning" OR "Learning, Deep" OR "Hierarchical Learning" OR "Learning, Hierarchical" OR "Machine Learning" OR "Learning, Machine" OR "Transfer Learning" OR "Learning, Transfer") AND ("asynchronous service models" OR "remote technologies" OR "remote technology" OR "virtual platform" OR "virtual platforms" OR "Mobile-phone-based screening" OR "Mobile Applications" OR "Application, Mobile" OR "Applications, Mobile" OR "Mobile Application" OR "Mobile Apps" OR "App, Mobile" OR "Apps, Mobile" OR "Mobile App" OR "Portable Electronic Apps" OR "App, Portable Electronic" OR "Apps, Portable Electronic" OR "Electronic App, Portable" OR "Electronic Apps, Portable" OR "Portable Electronic App" OR "Portable Electronic Applications" OR "Application, Portable Electronic" OR "Applications, Portable Electronic" OR "Electronic Application, Portable" OR "Electronic Applications, Portable" OR "Portable Electronic Application" OR "Portable Software Apps" OR "App, Portable Software" OR "Apps, Portable Software" OR "Portable Software App" OR "Software App, Portable" OR "Software Apps, Portable" OR "Portable Software Applications" OR "Application, Portable Software" OR "Applications, Portable Software" OR "Portable Software Application" OR "Software Application, Portable" OR "Software Applications, Portable" OR "Computer Software" OR "Software, Computer" OR "Computer Programs" OR "Computer Program" OR "Program, Computer" OR "Programs, Computer" OR "Software Tools" OR "Software Tool" OR "Tool, Software" OR "Tools, Software" OR "Computer Applications Software" OR "Applications Software, Computer" OR "Applications Softwares, Computer" OR "Computer Applications Softwares" OR "Software, Computer Applications" OR "Softwares, Computer Applications" OR "Computer Software Applications" OR "Application, Computer Software" OR "Applications, Computer Software" OR "Computer Software Application" OR "Software	5

(continued)

S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
	Application, Computer" OR "Software Applications, Computer" OR "Applications, Medical Informatics" OR "Informatics Applications, Medical" OR "Application, Medical Informatics" OR "Informatics Application, Medical" OR "Medical Informatics Application" OR "Computer Programs and Programming" OR "Software Engineering" OR "Engineering, Software" OR "virtual consultation" OR "virtual consultations" OR "Virtual online consultation" OR "Virtual online consultations" OR "Virtual Care" OR "E-consultation" OR "e-referral" OR "remote consultation" OR tele-consultation OR "video-consultation"))) AND (Neoplasia OR Neoplasias OR Neoplasm OR Tumors OR Tumor OR Cancer OR Cancers OR Malignancy OR Malignancies OR "Malignant Neoplasms" OR "Malignant Neoplasm" OR "Neoplasm, Malignant" OR "Neoplasms, Malignant" OR "Benign Neoplasms" OR "Neoplasms, Benign" OR "Benign Neoplasm" OR "Neoplasm, Benign") AND ("Systematic Review" OR "Meta-analysis" OR "Metanalysis" OR "Meta analysis")	
SCIELO	(Diagnoses OR Diagnose OR "Oral cancer diagnosis" OR "computer-aided diagnosis" OR "Cancer Early Detection" OR "Cancer Screening" OR "Cancer Screening Test" OR "Early Diagnosis of Cancer" OR "Cancer Early Diagnosis") AND ((Algorithm OR Algorithms OR "Intelligence, Artificial" OR "Computational Intelligence" OR "Machine Intelligence" OR "Computer Reasoning" OR "AI (Artificial Intelligence)" OR “computer-assisted diagnosis (CAD)” OR “(CAD)” OR “Diagnosis, Computer Assisted” OR “Computer-Assisted Diagnosis” OR “Computer Assisted Diagnosis” OR “Computer-Assisted Diagnoses” OR “Diagnoses, Computer-Assisted” OR "Computer Vision Systems" OR "Knowledge Acquisition (Computer)" OR "Computer Neural Network" OR "Computer Neural Networks" OR "Neural Network Model" OR "Neural Network Models" OR "Computational Neural Networks" OR "Computational Neural Network" OR "artificial neural network" OR "convolutional neural network" OR "Deep Learning" OR "Hierarchical Learning" OR "Machine Learning" OR "Transfer Learning") AND ("asynchronous service models" OR "remote technologies" OR "remote technology" OR "virtual platform" OR "virtual platforms" OR "Mobile-phone-based screening" OR "Mobile Applications" OR "Application, Mobile" OR "Applications, Mobile" OR "Mobile Application" OR "Mobile Apps" OR "Mobile App" OR "Portable Electronic Apps" OR "Portable Electronic App" OR "Portable Electronic Applications" OR "Portable Electronic Application" OR "Portable Software Apps" OR "Portable Software Applications" OR "Portable Software Application" OR "Computer Programs" OR "Computer Program" OR "Software Tools" OR "Software Tool" OR "Computer Applications Software" OR "Computer Applications Softwares" OR "Computer Software Applications" OR "Computer Software Application" OR "Medical Informatics Application" OR "Computer Programs and Programming" OR "Software Engineering" OR "virtual consultation" OR "virtual consultations" OR "Virtual online consultation" OR "Virtual online consultations" OR "Virtual Care" OR "E-consultation" OR "e-referral" OR "remote consultation" OR tele-consultation OR "video-consultation")) AND (Neoplasia OR Neoplasias OR Neoplasm OR Tumors OR Tumor OR Cancer OR Cancers OR Malignancy OR Malignancies OR "Malignant Neoplasms" OR "Malignant Neoplasm" OR "Benign Neoplasms" OR "Benign Neoplasm") AND ("Systematic Review" OR "Meta-analysis" OR "Metanalysis" OR "Meta analysis")	0
PROQUEST	noft(diagnoses OR diagnose OR "Diagnoses and Examinations" OR "Examinations and Diagnoses" OR "Postmortem Diagnosis" OR "Diagnoses, Postmortem" OR "Diagnosis, Postmortem" OR "Postmortem Diagnoses" OR "Antemortem Diagnosis" OR "Antemortem Diagnoses" OR "Diagnoses, Antemortem" OR "Diagnosis, Antemortem" OR "Oral cancer diagnosis" OR "computer-aided diagnosis" OR " Cancer Early Detection" OR "Cancer Screening" OR "Screening, Cancer" OR "non-invasive screening" OR "Cancer Screening Tests" OR "Cancer Screening Test" OR "Screening Test, Cancer" OR "Screening Tests, Cancer" OR "Test, Cancer Screening" OR "Tests, Cancer Screening" OR "Early Diagnosis of Cancer" OR "Cancer Early Diagnosis") AND noft(((Algorithm OR Algorithms OR "Intelligence, Artificial" OR "Computational Intelligence" OR "Intelligence, Computational" OR "Machine Intelligence" OR "Intelligence, Machine" OR "Computer Reasoning" OR "Reasoning, Computer" OR "AI	1

(continued)

S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
	(Artificial Intelligence)" OR "computer-assisted diagnosis (CAD)" OR "(CAD)" OR "Diagnosis, Computer Assisted" OR "Computer-Assisted Diagnosis" OR "Computer Assisted Diagnosis" OR "Computer-Assisted Diagnoses" OR "Diagnoses, Computer-Assisted" OR "Computer Vision Systems" OR "Computer Vision System" OR "System, Computer Vision" OR "Systems, Computer Vision" OR "Vision System, Computer" OR "Vision Systems, Computer" OR "Knowledge Acquisition (Computer)" OR "Acquisition, Knowledge (Computer)" OR "Knowledge Representation (Computer)" OR "Knowledge Representations (Computer)" OR "Representation, Knowledge (Computer)" OR "Computer Neural Network" OR "Computer Neural Networks" OR "Network, Computer Neural" OR "Networks, Computer Neural" OR "Neural Network, Computer" OR "Models, Neural Network" OR "Model, Neural Network" OR "Network Model, Neural" OR "Network Models, Neural" OR "Neural Network Model" OR "Neural Network Models" OR "Computational Neural Networks" OR "Computational Neural Network" OR "Network, Computational Neural" OR "Networks, Computational Neural" OR "Neural Network, Computational" OR "Neural Networks, Computational" OR "artificial neural network" OR "convolutional neural network" OR "Deep Learning" OR "Learning, Deep" OR "Hierarchical Learning" OR "Learning, Hierarchical" OR "Machine Learning" OR "Learning, Machine" OR "Transfer Learning" OR "Learning, Transfer") AND ("asynchronous service models" OR "remote technologies" OR "remote technology" OR "virtual platform" OR "virtual platforms" OR "Mobile-phone-based screening" OR "Mobile Applications" OR "Application, Mobile" OR "Applications, Mobile" OR "Mobile Application" OR "Mobile Apps" OR "App, Mobile" OR "Apps, Mobile" OR "Mobile App" OR "Portable Electronic Apps" OR "App, Portable Electronic" OR "Apps, Portable Electronic" OR "Electronic App, Portable" OR "Electronic Apps, Portable" OR "Portable Electronic App" OR "Portable Electronic Applications" OR "Application, Portable Electronic" OR "Applications, Portable Electronic" OR "Electronic Application, Portable" OR "Electronic Applications, Portable" OR "Portable Electronic Application" OR "Portable Software Apps" OR "App, Portable Software" OR "Apps, Portable Software" OR "Portable Software App" OR "Software App, Portable" OR "Software Apps, Portable" OR "Portable Software Applications" OR "Application, Portable Software" OR "Applications, Portable Software" OR "Portable Software Application" OR "Software Application, Portable" OR "Software Applications, Portable" OR "Computer Software" OR "Software, Computer" OR "Computer Programs" OR "Computer Program" OR "Program, Computer" OR "Programs, Computer" OR "Software Tools" OR "Software Tool" OR "Tool, Software" OR "Tools, Software" OR "Computer Applications Software" OR "Applications Software, Computer" OR "Applications Softwares, Computer" OR "Computer Applications Softwares" OR "Software, Computer Applications" OR "Softwares, Computer Applications" OR "Computer Software Applications" OR "Application, Computer Software" OR "Applications, Computer Software" OR "Computer Software Application" OR "Software Application, Computer" OR "Software Applications, Computer" OR "Applications, Medical Informatics" OR "Informatics Applications, Medical" OR "Application, Medical Informatics" OR "Informatics Application, Medical" OR "Medical Informatics Application" OR "Computer Programs and Programming" OR "Software Engineering" OR "Engineering, Software" OR "virtual consultation" OR "virtual consultations" OR "Virtual online consultation" OR "Virtual online consultations" OR "Virtual Care" OR "E-consultation" OR "e-referral" OR "remote consultation" OR tele-consultation OR "video-consultation"))) AND noft(Neoplasia OR Neoplasias OR Neoplasm OR Tumors OR Tumor OR Cancer OR Cancers OR Malignancy OR Malignancies OR "Malignant Neoplasms" OR "Malignant Neoplasm" OR "Neoplasm, Malignant" OR "Neoplasms, Malignant" OR "Benign Neoplasms" OR "Neoplasms, Benign" OR "Benign Neoplasm" OR "Neoplasm, Benign") AND noft("Systematic Review" OR "Meta-analysis" OR "Metanalysis" OR "Meta analysis")	*(continued)*
Google Scholar	With all words: (Diagnose OR "Oral cancer diagnosis" OR "computer-aided diagnosis" OR "Cancer Early Detection") AND (("Intelligence, Artificial" OR "Machine Learning" OR "Deep Learning" OR "Neural Network Model" OR "convolutional neural network") AND ("remote technology" OR "virtual platform" OR "Mobile-phone-based screening"	39

S1 Table 1 - Database search strategy.

Database	Search (January the 12st, 2022)	References
	OR "Portable Software Application" OR "Mobile Application" OR "Mobile App" OR "Computer Software Application" OR "virtual consultation" OR "E-consultation" OR tele-consultation)) com a frase exata: "Systematic Review" OR "Meta-analysis" OR "Metanalysis" OR "Meta analysis" com no mínimo uma das palavras: Neoplasia OR Neoplasm OR Tumor OR Cancer OR "Malignant Neoplasm" OR "Benign Neoplasm"	
JSTOR	*("Cancer Early Detection") AND ("Artificial Intelligence ") AND ("Mobile Application" OR "Computer Software Application") AND (Neoplasia OR Neoplasm) AND ("Systematic Review")*	0

(continued)

S2 Table 1- Excluded articles and reasons for exclusion (n=23).

Author, year	Reasons for exclusions
Bartosch-Härlid A. (1) 2008.	14
Nayantara PV. (2) 2020.	14
Herman RA . (3), 2012	14
Simões PW . (4), 2015	06
Kourou K . (5), 2021	07
Drouin SJ. (6), 2013	10
Gudigar A. (7), 2020	02
Mahmood H. (8), 2020	11
Alsalem MA. (9), 2018	06
Abraha I. (10), 2018	02
Abbod MF . (11), 2007	06
Tian Y . (12), 2018	15
Yassin NIR. (13), 2018	05
Valente IR. (14), 2016	14
Amir GJ. (15), 2019	14
Robinson C. (16), 2008	14
Staal FCR. (17), 2021	14
Ursprung S. (18), 2020	3
Rajgor AD. (19), 2021	16
Badrigilan S. (21), 2021	3
Limardo A. (14), 2021	16
Taylor P. (16),	14
Noble, M. (17)	14

1 - Studies evaluating diagnosis of areas other than medicine and dentistry (Physiotherapist, Nutritionist, Nurse, Caregivers etc.); 2 – Patients with a confirmed diagnosis of cancer; 3 - Systematic Reviews not evaluating the diagnostic accuracy Artificial intelligence, Machine learning, Deep learning and Convolutional Neural Networks; 4 - Systematic Reviews with Artificial intelligence use for other diseases diagnosis (Diabetes, Hypertension, etc); 5 - Systematic reviews in which AI was not compared to a reference test; 6 - Systematic reviews evaluating other technologies for early detection or cancer diagnosis (spectrometry, biomarkers, autofluorescence, Multispectral widefield optical imaging, optical instruments, robotic equipment etc.); 7 - literature reviews, integrative reviews, narrative reviews, overviews; 8 - Editorials/Letters; 9 - Conferences, Summaries, abstracts and posters; 10 - In vitro studies; 11 - Studies of animal models; 12 - Thesis and Dissertations and book chapters; 13 - Pipelines, guidelines and research protocols; 14 - Review papers that do not follow the inclusion criteria adopted for the definition of Systematic Reviews; 15 - Primary studies of any type; 16 - No full paper avaliable.

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review and meta-analysis. Eur Radiol. 2020; 30(6):3558-3566. DOI: 10.1007/s00330-020-06666-3.
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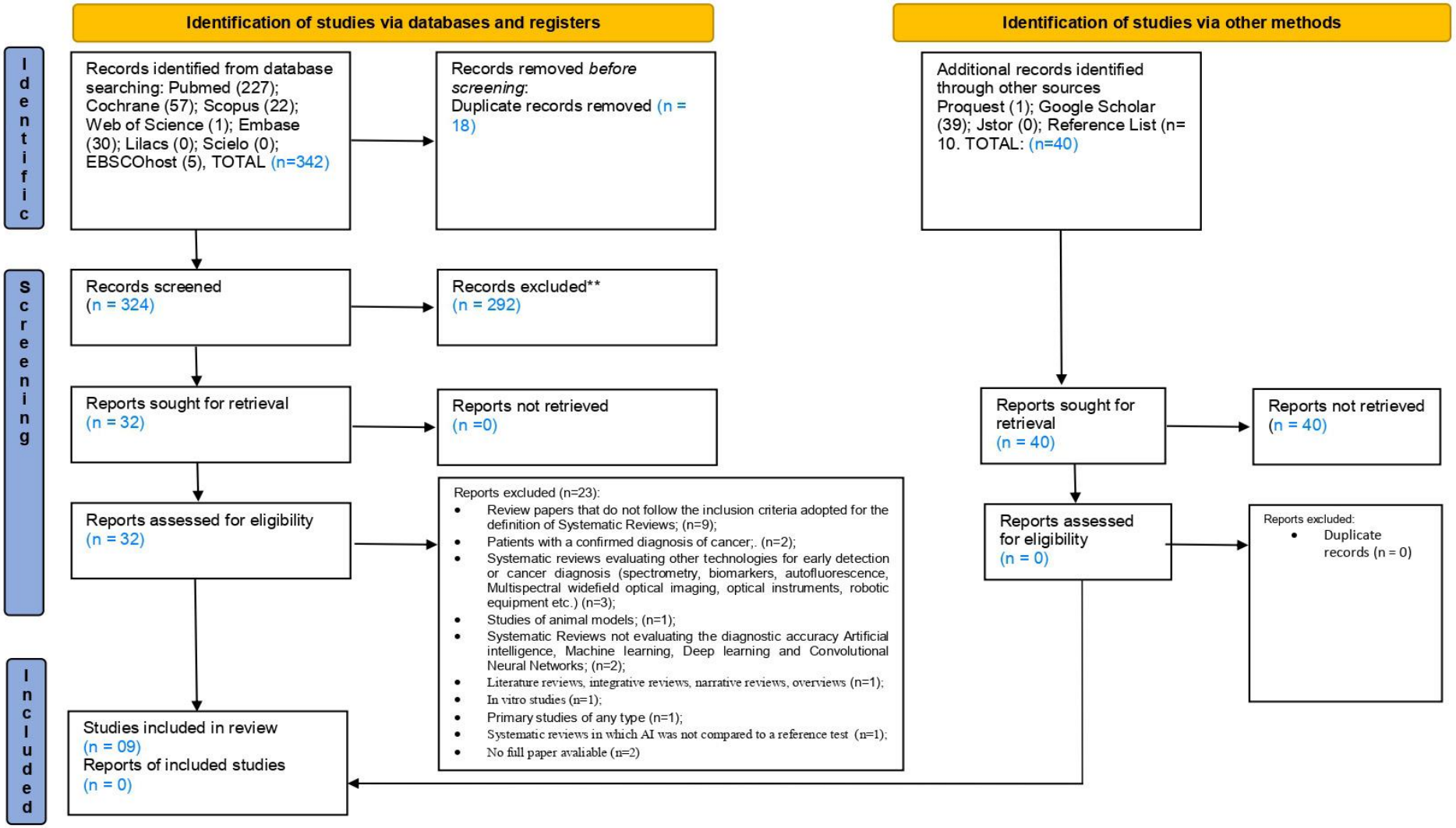

Figure: 1 - Flow diagram of the literature search and selection criteria

S3 Table 1- Over Laping (n=09).

Author, year	Included Studies	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Dorrius et al, 2011,	10	Arazi-Kleinman 2009	Meeuwis 2009	Baltzer 2009	Baltzer 2009	Veltman [2009	Renz 2008	Hauth 2008	Williams 2006	Lehman 2005	Kelcz 2002				
Nindrea et al, 2018,	11	Chang et al., 2003	Polat and Gunes, 2007	Heidari et al., 2018	Ayer et al., 2010	Dramicanin et al., 2012	Subramanian et al., 2014	Mert et al., 2015	Milosevic et al., 2015	Sun et al., 2015	Asri et al., 2016	Akay, 2009			
Eadie et al, 2012,	48	Andre M, et al 2007	Awai K, et al 2006	Ayer T, et al 2010	Balleyguier C, et all 2005	Brem RF, et al 2001	Chang W-L, et al 2010	Chen H, et al 2010	Choi EJ, et al 2008	Ciatto S,et al 2003	Claridge E, et al 1992	Fenton JJ, et al 2007	Helm EJ, et al 2009	Horsch K, et al 2006	Horsch K, et al 2004
		Karahaliou AN, et al 2008	Kegelmeyer WP, et al 1994	Lauria A. et al 2009	Lee IJ,, et al 2005	Leichter I, et all 2000	Leichter I, et al 2000	Llobet R, et al 2007	Lo JY, et al 1995	Mani A, et al 2004	Marx C, et al 2004	Matake K, et al 2006	Meeuwis C, et al 2010	Moore W, et al 2010	Morimoto T, et al 2008
		Seidenari S, et al 1998	Shen WC, et al 2007	Shi X, et al 2010	Stanganelli I,, et al 2005	Szucs-Farkas Z,, et al 2010	Taylor SA, et al 2008	Van den Biggelaar FJHM,, et al 2010	van Beek EJR,, et al 2008	Vergnaghi D, et al 2001	Wang Y, et al 2010	Yu YH,, et al 2008	Zhang J, et al 2007	Jiang YL, et al 2006	Juntu J, et al 2010
		Huo ZM, et al 2002	Huo ZM, et al 2002	Huo ZM, et al 2002	Jesneck JL, et al 2007	Jesneck JL, et al 2007									
Zhao et al, 2019	5	Jeong et al 2018	Gitto et al 2018	Yoo et al 2018	Gao et al 2017	Choi et al 2016									
Azavedo et al, 2012	4	Gilbert et al., 2008	Gromet et al., 2008	Georgian-Smith et al., 2007	Khoo et al., 2005										
Cuocolo et al, 2020	12	Abraham et al (2019)	Antonelli et al (TZ) Antonelli et al (PZ) 2019	Bonekamp et al 2018	Chaddad et al 2018	Chen et al 2019	Dikaios et al (PZ) Dikaios et al (TZ) 2015	Fehr et al 2015	Le et al 2017	Li et al 2018	Sobecki et al 2018	Toivonen et al 2019	Zhong et al 2019		
Xing et al, 2021	15	Artan 2010	Bonekamp 2018	Giannini 2015	Giannini 2016	Kwak 2015	Litjens 2014	Liu 2013	Puech 2007	Roethke 2016	Thon 2017	Vos 2012	Wang 2017	Yang 2017	Zhao 2015
Tabatabaei et al, 2021,	18	Cui et al., 2018d	Chen et al., 2020	Xiao et al., 2019	Wu et al., 2018	Vamvakas et al., 2019	Lu et al., 2018	Hashido et al., 2020	Cho et al., 2018	Lin et al., 2017	Cho et al., 2017	Takahashi et al., 2019	Park et al., 2019	Wang et al., 2019	Tian et al., 2018
		Gao et al., 2020	Çinarer et al., 2020	Bi et al., 2019	Zhong 2018	Zhong 2018									
Henriksen EL 2018	13	Dean JC 2006	Ko JM 2006	Morton MJ 2006	Fenton JJ 2007	Fenton JJ 2011	Gomez SS 2011	Fenton JJ 2013	Lehman CD 2015	Gilbert FJ 2008	Romero C 2011	Bargallo X 2014	Georgian-Smith D 2007	Gromet M 2008	

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2/3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3/5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provideregistration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered,language, publication status) used as criteria for eligibility, giving rationale.	6/7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identifyadditional studies) in the search and date last searched.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could berepeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processesfor obtaining and confirming data from investigators.	7/8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions andsimplifications made.	7
Risk of bias in individualstudies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this wasdone at the study or outcome level), and how this information is to be used in any data synthesis.	8/9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10/15
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	16
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	21
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	22/27
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	27
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	27
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097 For more information, visit: **www.prisma-statement.org.**

Table 1: 1 - Summary of descriptive characteristics of included articles (n=09).

Author, year, country and design studies	Included Studies	Type of cancer	Index test	Reference test	True positives / N of images	True Negatives /N of images	Sensitivity and Specificity/ odds ratio, Mean±SD, *p' value*	Diagnostic accuracy (%) , Mean±SD, *p' value*	Conclusions
Dorrius et al, 2011, Netherlands, Descriptives studies	10	Breast Cancer	Computer-aided-detection (CADe)	Magnetic Resonance Imaging (MRI)	-	-	Sensitivity Radiologist no CAD, general 82% (95% CI: 72%–90%) Radiologist with CAD, general 89% (95% CI: 83%–93%) Specificity Radiologist no CAD, general 81% (95% CI: 74%–87%) Radiologist with CAD, general 81% (95% CI: 76%–85%)	-	MR images CAD has little influence on the sensitivity and specificity of the performance of radiologists experienced in breast MRI diagnosis. Breast MRI interpretation by radiologists remains essential. Radiologists with less experience seem to benefit from a CAD system when performing breast MRI evaluation.

(Continued)

Table 1. (Continued)

Author, year, country and design studies	Included Studies	Type of cancer	Index test	Reference test	True positives / N of images	True Negatives /N of images	Sensitivity and Specificity/ odds ratio, Mean±SD, *p' value*	Diagnostic accuracy (%) , Mean±SD, *p' value*	Conclusions
Henriksen EL et al, (2018), Denmark Clinical trials	13	Breast cancer	CAD system.; Single Reading (SR) SR vs SR + CAD; Double Reading (DR) DR vs SR þ CAD;	MM	-	-	-	-	In conclusion, all but two studies found that SR CAD improves mammography screening RRs, sensitivity, and CDR when compared to SR alone. No statistically significant variations in sensitivity or CDR were seen when compared to DR. More research is needed to assess the impact of CAD in a population-based screening program with high-volume readers. Longer follow-up studies are required for a thorough assessment of cancer rates. And studies based on digital mammography are required to assess the efficacy of CAD in the current standard of care technology.

(Continued)

Table 1. (Continued)

Author, year, country and design studies	Included Studies	Type of cancer	Index test	Reference test	True positives / N of images	True Negatives /N of images	Sensitivity and Specificity/ odds ratio, Mean±SD, *p' value*	Diagnostic accuracy (%) , Mean±SD, *p' value*	Conclusions
Nindrea et al, 2018, Indonesia, Diagnostic Accuracy studies	11	Breast cancer	Machine Learning Algorithms Super Vector Machine (SVM); Artificial Neural Networks (ANN); Decision Tree (DT); Naive Bayes (NB); K-Nearest Neighbor (KNN)	Mammography (MM)	SVM 40,37%/3532; ANN 1,30%/63325 DT 33,19%/738 NB 35,32%/1039 KNN 41%/1568	SVM 46,40%/3532 ANN 97,88%/63325 DT 61,38%/738 NB 54,66%/1039 KNN 44,89%/1568	Sensitivity SVM: 0.67–0.99 (95% CI: ([0.41-0.87]-[0.95–1.00]); ANN: 0.84–0.97 (95% CI: ([0.60-0.97]-[0.95–98]); DT: 0.90-0.92 (95% CI: ([0.68-0.99]-[0.88–.95]); NB: 0.76-0.91 (95% CI: ([0.68-0.83]-[0.87–.95]); KNN: 0.56-0.95 (95% CI: ([0.48-0.64]-[0.92–0.97]); Specificity SVM: 0.60-0.98 (95% CI: ([0.36-0.81]-[0.96–1.00]); ANN: 0.71-0.99 (95% CI: ([0.48-0.89]-[0.99–0.99]); DT: 0.79-0.97 (95% CI: ([0.54-0.94]-[0.9–0.98]); NB: 0.78-0.99 (95% CI: ([0.52-0.94]-[0.9–1.00]); KNN: 0.53–0.99 (95% CI: ([0.44-0.61]-[0.93–0.97);	SVM: 99.51 %; ANN: 97.3%; DT: 95.13%; NB: 95.99%; KNM: 95.27%;	Therefore, the early diagnosis of breast cancer will be more effective, and the mortality rate of breast cancer will decrease. Additionally, if the present method is designed in the form of a web-based or smartphone application, women who want to know their own risk of breast cancer will be able to access this information easily in daily life.

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Table 1. (Continued)

Author, year, country and design studies	Included Studies	Type of cancer	Index test	Reference test	True positives / N of images	True Negatives /N of images	Sensitivity and Specificity/ odds ratio, Mean±SD, *p' value*	Diagnostic accuracy (%) , Mean±SD, *p' value*	Conclusions
Azavedo et al, 2012, Sweden, Prospective or Retrospective studies	4	Breast cancer	Computer-aided-detection (CAD)	MM	-	-	-	-	The scientific evidence is insufficient to determine whether CAD + single reading by one breast radiologist would yield results that are at least equivalent to those obtained in standard practice, i.e. double reading where two breast radiologists independently read the mammographic images.
Eadie et al, 2012, United Kingdom, Diagnostic Accuracy studies	48	Breast cancer, lung cancer, liver cancer, prostate cancer, bone cancer, bowel cancer, skin cancer, neck cancer.	CADe; Diagnostic CAD (CADx)	MM; Breast ultrasound (BUS); BUS + mammogram; Lung Conputered Tomography (LCT); Dermatologic;	-	-	Sensitivity (SD) CADe overall Radiologist alone: 80.41±1.46 With CAD: 84.02±1.30 CADx overall Radiologist alone: 2.79±6.12 With CAD: 90.66±4.07 Specificity (SD) CADe overall Radiologist alone: 90.10±1.97 With CAD: 87.08±2.75 CADx overall Radiologist alone: 83.00±14.46) With CAD: 88.04±15.03	Diagnostic odds ratio (DOR) (SD) CADe overall Radiologist alone 3.63±0.16 With CAD: 3.58±0.20 CADx overall Radiologist alone 3.44±0.79 With CAD : 4.75±0.91	Certain types of CAD did offer diagnostic benefit compared with radiologists diagnosing alone: significantly better ln DOR scores were seen with CADx systems used with mammography and breast ultrasound. Applications such as lung CT and dermatologic imaging do not seem to benefit overall from the addition of CAD. These findings therefore offer suggestions about how CAD can be best applied in the diagnosis of cancer using imaging.

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Table 1. (Continued)

Author, year, country and design studies	Included Studies	Type of cancer	Index test	Reference test	True positives / N of images	True Negatives /N of images	Sensitivity and Specificity/ odds ratio, Mean±SD, *p' value*	Diagnostic accuracy (%) , Mean±SD, *p' value*	Conclusions
Zhao et al, 2019, China, Prospective or Retrospective studies	5	Thyroid (nodules) cancer	CADx system	US	positive likelihood ratio CADx system 4.1 (95% CI 2.5–6.9); CADx by Samsung 4.9 (95% CI 3.4– 7.0); radiologists 11.1 (95% CI 5.6–21.9);	negative likelihood ratio CADx sistem 0.17 (95% CI 0.09–0.32); CADx by Samsung 0.22 (95% CI 0.12–0.38); radiologists 0.13 (95% CI 0.08–0.21);	Sensitivity CADx system 0.87 (95% CI: 0.73–0.94; I^2 = 93.53%); CADx by Samsung 0.82 (95% CI: 0.69–0.91; I^2 = 79.62%); radiologists 0.88 (95% CI: 0.80–0.93; I^2 = 81.66%); Specificity CADx system 0.79 (95% CI: 0.63–0.89; I^2 = 89.67 %); CADx by Samsung 0.83 (95% CI: 0.76–0.89; I^2 = 27.52%); radiologists 0.92 (95% CI: 0.84– 0.96; I^2 = 84.25%);	DOR CADx system 25 (95% CI: 15–42; I^2 = 15.5%, p=0.315); CADx by Samsung 23 (95% CI: 11–46; I^2 =35.9% ,p=0 .197); radiologists 86 (95% CI: 47–158; I^2 =41.1%, p= 0.147)	The sensitivity of the CAD system in thyroid nodules was similar to that of experienced radiologists. However, the CAD system had lower specificity and DOR than the experienced radiologist. The CAD system may play the potential role as a decision-making assistant alongside radiologists in the thyroid nodules' diagnosis.

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Table 1. (Continued)

Author, year, country and design studies	Included Studies	Type of cancer	Index test	Reference test	True positives / N of images	True Negatives /N of images	Sensitivity and Specificity/ odds ratio, Mean±SD, *p' value*	Diagnostic accuracy (%) , Mean±SD, *p' value*	Conclusions
Cuocolo et al, 2020, Italy, Diagnostic Accuracy studies	12	PCa	Machine learning (ML) ANN ; SVM; LDA; NB; Linear regression (LIR); Random forest (RF); Logistic regression (LOR); Convolutional neural network (CNN); Deep transfer learning (DTL);	MRI	-	-	ML in PCa identification – overall (95%CI: 0.81–0.91; I^2 = 92%, p <0.0001); Biopsy group (95%CI: 0.79–0.91; I^2 = 87%, p <0.0001); Radical prostatectomy group (95%CI: 0.76– 0.99; I^2 = 93%, p <0.0001); Deep learning (95%CI: 0.69–0.86; I^2 = 86%, p = 0.0001); Non-deep learning (95%CI: 0.85– 0.94; I^2 = 89%, p <0.0001);	AUC overall AUC = 0.86 Biopsy group AUC= 0.85; Rradical prostatectomy group AUC = 0.88; Deep learning AUC = 0.78; Non-deep learning AUC = 0.90;	The findings show promising results for quantitative ML-based identification of csPCa. The results suggest that the overall accuracy of ML approached might be comparable with that reported for traditional Prostate Imaging Reporting and Data System scoring. Nevertheless, these techniques have the potential to improve csPCa detection accuracy and reproducibility in clinical practice.

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Table 1. (Continued)

Author, year, country and design studies	Included Studies	Type of cancer	Index test	Reference test	True positives / N of images	True Negatives /N of images	Sensitivity and Specificity/ odds ratio, Mean±SD, *p' value*	Diagnostic accuracy (%) , Mean±SD, *p' value*	Conclusions
Tabatabaei et al, 2021, USA Retrospectives studies	18	Glioma	DT; KNN; SVM; RF; LOR; LDA; LIR; Least Absolute Shrinkage and Selection Operator (LAS/SO); Elastic Net (EN); Gradient Descent Algorithm (GDA); Deep Neural Network (DNN)	MRI	-	-	-	-	The results appear promising for grade prediction from MR images using the radiomics techniques. However, there is no agreement about the radiomics pipeline, the number of extracted features, MR sequences, and machine learning technique. Before the clinical implementation of glioma grading by radiomics, more standardized research is needed.

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Table 1. (Continued)

Author, year, country and design studies	Included Studies	Type of cancer	Index test	Reference test	True positives / N of images	True Negatives /N of images	Sensitivity and Specificity/ odds ratio, Mean±SD, *p' value*	Diagnostic accuracy (%) , Mean±SD, *p' value*	Conclusions
Xing et al, 2021, China, Retrospective studies	15	prostate cancer (PCa) ; Peripheral zone (PZ); Transitional zone (TZ); Central gland (CG);	CAD system.; ANN; SVM; Linear Discriminant Analysis (LDA); Radiomic Machine Learning (RML); Non--specific classifier (NSC);	MRI	SVM 42,76%/608; ANN 34,55%/301; RML 34,78%/738; NSC 19,41%/1586; PZ 51,95%/256; TZ 59,67%/186; CG 32,39%/71;	SVM 41,94%/608; ANN 37,54%/301; RML 32,60%/738; NPC 65,15%/1586; PZ 32,81%/256; TZ 26,34%/186; CG 46,47%/71;	Sensitivity: 0.47 to 1.00 0.87(95% CI: 0.76–0.94; I^2=90.3%, *p*=0.00) ANN: 0.66 to 0.77 SVM: 0.87 to 0.92 LDA: NR RML: 0.96 Prostate zones PZ: 0.66 to 1.00 TZ: 0.89 to 1.00 CG: 0.66 Specificity: 0.47 to 0.89 0.76(95% CI: 0.62–0.85; I^2=*95.8%, p* =0.00) ANN: 0.64 to 0.92 SVM: 0.47 to 0.95 LDA: NR RML: 0.51 Prostate zones PZ :0.48 to 0.89; TZ:0.38 to 0.85; CG:0.92	AUC 0.89 (95% CI: 0.86–0.91)	The study indicated that the use of CAD systems to interpret the results of MRI had high sensitivity and specificity in diagnosing PCa. We believe that SVM should be recommended as the best classifier for the CAD system.

Subtitles: CADe = Computer-aided-detection; MRI = Magnetic Resonance Imaging; SVM = Super Vector Machine; ANN = Artificial Neural Networks; DT = Decision Tree; NB = Naive Bayes; KNN = K-Nearest Neighbor; MM = Mammography; CADx = Diagnostic CAD; BUS = Breast ultrasound; DOR = Diagnostic odds ratio; LCT = Lung Conputered Tomography; CDR = CAD on cancer detection rate (CDR); DR = double reading; RR = Recall Rate; Pca = Prostate cancer; PZ = Peripheral zone; TZ = Transitional zone; CG = Central gland; LDA = Linear Discriminant Analysis; RML=Radiomic Machine Learning; NSC = Non--specific classifier; ML= Machine learningA; LIR = Linear regression; RF = Random forest; LOR = Logistic regression; CNN = Convolutional neural network; DTL=Deep transfer learning; LAS/SO = Least Absolute Shrinkage and Selection Operator; EN = Elastic Net; GDA = Gradient Descent Algorithm; DNN = Deep Neural Network; SR=Single Reading; DR= Double Reading;

Table 2: 2- Evaluation of methodological quality of included Systematic Reviews (n=9)

Study	Methodological quality items assessed											Overall quality[a]
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	
Dorrius (2011)	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	High
Nindrea (2018)	N	Y	Y	Y	Y	Y	Y	U	N	Y	N	Moderate
Eadie (2012)	N	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	High
Zhao (2019)	N	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	High
Henriksen (2019)	Y	Y	Y	Y	Y	N	Y	Y	N	U	U	Moderate
Azavedo (2012)	N	Y	Y	Y	Y	Y	U	N	N	Y	Y	Moderate
Cuocolo (2020)	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	High
Xing (2021)	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	High
Tabatabaei (2021)	N	U	Y	Y	Y	U	U	U	N	Y	U	Low

Note: JBI Critical Appraisal Tool for Systematic Reviews - Q1. Is the review question clearly and explicitly stated? Q2. Were the inclusion criteria appropriate for the review question? Q3. Was the search strategy appropriate? Q4. Were the sources and resources used to search for studies adequate? Q5. Were the criteria for appraising studies appropriate? Q6. Was critical appraisal conducted by two or more reviewers independently? Q7. Were there methods to minimize errors in data extraction? Q8. Were the methods used to combine studies appropriate? Q9. Was the likelihood of publication bias assessed? Q10. Were recommendations for policy and/or practice supported by the reported data? Q11. Were the specific directives for new research appropriate?

[a]Low quality: 1 to 5 “yes” answers; Moderate quality: 6 to 10 “yes” answers; High quality: 11 to 13 “yes” answers;

Abbreviations: N, no; U, unclear; Y, yes

CAPÍTULO 5 - DISCUSSÃO GERAL E CONCLUSÕES

5.1 DISCUSSÃO GERAL

A interrupção das atividades odontológicas pelas autoridades de saúde, em consequência da pandemia de COVID-19, levou a uma diminuição no atendimento de pacientes oncológicos que necessitam de tratamento, focando apenas em emergências. Houve também, uma redução significativa no atendimento odontológico, na manutenção periodontal e no atendimento ao paciente na clínica de doenças bucais. No entanto, essa queda foi gradativamente compensada pelo crescente serviço de TM. Nesse contexto, houve um aumento da abstenção dos pacientes às consultas para evitar o risco de infecção. Este fato foi acentuado pelas medidas restritivas das autoridades de saúde para proteger os pacientes de risco e funcionários. Após um período médio de 4 semanas de atividade mínima, observou-se um aumento no fluxo de pacientes, provavelmente devido ao aumento da demanda por atendimento odontológico de emergência, apesar do número crescente de pacientes ativos com COVID-19 e mortes relacionadas durante a pandemia [1]. No entanto, essa queda foi gradativamente compensada pelo crescente serviço de TM.

De acordo com Barca et al [2], a TM é bem aceita por pacientes e profissionais de saúde, principalmente, pelos pacientes que residem em áreas bastante distantes das unidades de saúde, que precisam percorrer longas distâncias e, principalmente, estarem expostos a outros pacientes que podem ser portadores de COVID-19 e outros agentes infecciosos. A TM pode ter subáreas, como a TO, que aplicada ao acompanhamento de pacientes com câncer oral (CO) e câncer de cabeça e pescoço (CCP) foi uma ferramenta útil no suporte aos pacientes, especialmente durante o período de pandemia, com melhoria do bem-estar geral e da QV. Os benefícios apresentados pelo uso da TO foram a continuidade do

atendimento odontológico, redução de deslocamentos ao hospital para atendimento de pacientes, redução do risco de infecção pelo coronavírus e limitação de consultas presenciais para proteção dos profissionais de saúde [3].

A TO trouxe vantagens não apenas durante a pandemia de COVID-19, porque atinge outros aspectos da assistência odontológica, beneficiando pacientes em diversas situações. Ao oferecer suporte especializado de grande escala e baixo custo às unidades básicas de saúde públicas, a TO garante o acesso à tecnologia por pessoas de baixa renda, o que otimiza o atendimento, reduz o tempo de espera por consulta e aumenta a resolutividade do caso clínico [4]. Atividades como aconselhamento pré-operatório adicional, educação sobre cuidados pós-operatórios, aconselhamento dietético e recomendações de exercícios para o pescoço e ombros podem ser fornecidas pela TO [5].

Embora autores como Barca et al [2] corroborem com a TO, a literatura apresenta controvérsias. Entretanto, a TO no acompanhamento de pacientes com CO e de CCP apresenta desafios que precisam ser superados. A falta de aceitação da TO pelos cirurgiões-dentistas é atribuída a sua complexidade e resistência à aquisição de novas habilidades [6,7]. Eles são desafiados tecnologicamente, com medo de fazer uma avaliação de caso imprecisa e preocupados com o aumento de custos e despesas. Há restrições relacionadas à infraestrutura, como acesso precário à internet, escassez de hardware, falta de treinamento, de suporte técnico e expertise. A incompatibilidade organizacional da TO com o sistema de saúde, o reembolso financeiro insuficiente, as diretrizes inadequadas na coordenação entre o centro remoto e a central e o alto custo de instalação são outros desafios relacionados à sua aceitação pelos dentistas [7].

A representação bidimensional das lesões e a incapacidade de realizar testes como palpação, percussão e ausculta são outras limitações [8]. Mesmo com a tecnologia de imagem, é um desafio visualizar certas áreas da mucosa [9]. O acesso às informações do paciente é uma das principais limitações que podem afetar a validade da TO. A falta de informação pode diminuir a confiança do cirurgião-dentista em fazer um diagnóstico usando apenas um sistema de TO e, portanto, diminuir o seu escore de validade [10].

Neste contexto, há uma diferença entre os benefícios do uso da TO e do exame clínico presencial. Nessas situações, a TO tem o potencial de garantir apenas um ajuste temporário até que o exame clínico seja possível de ser realizado

presencialmente. No caso da não aceitação da TO pelos pacientes, a dificuldade de comunicação face a face leva o paciente a apreensão quanto à inadequação da comunicação de seus problemas aos seus dentistas. A aceitabilidade da TO pelos pacientes aumentará em paralelo com a aceitabilidade da TM em geral, que está aumentando a cada dia [11,12].

Deve-se destacar que check-ups, aconselhamento e suporte constantes podem ser realizados por meio de consultas de TO para manter e melhorar o bem-estar geral dos pacientes e, consequentemente, a QV [13]. O contato, embora remoto, tem influenciado positivamente o estado de bem-estar, a motivação e a sensação de segurança do paciente, especialmente durante o período pandêmico [2]. Além disso, pode não só auxiliar na educação do paciente, mas também contribuir para o diagnóstico e tratamento [14] em associação com uma possível consulta presencial para um diagnóstico definitivo, quando necessário.

A TO também desempenhou um papel decisivo na redução do risco de disseminação do COVID-19. Durante o recente período de emergência sanitária, o tratamento do CCP [2] apresentou uma abordagem multidisciplinar (cirurgião maxilofacial, radioterapeuta, oncologista, nutricionista, etc.), através do envolvimento de outros especialistas por videoconferência e/ou fotografia. Deve-se notar que novos métodos, como a TO e a colaboração regional com outros centros, foram implementados com algum sucesso, a fim de atingir os tempos de espera almejados para a cirurgia precoce em casos mais urgentes em diferentes hospitais, com alívio do número de operações pendentes de CCP em 20% [5,15,16].

Existem limitações para consultas interativas de vídeo em tempo real no diagnóstico de doenças e avaliação dos problemas do paciente, particularmente no contexto odontológico. O modelo de TO tem algumas limitações, como a incapacidade de abordar a textura, tipo de tecido, coloração, profundidade da lesão e delinear claramente as bordas de uma lesão, principalmente na cavidade oral posterior, com conexão de dados não confiável e qualidade de imagem ruim. Fatores ligados ao paciente, como a capacidade de se conectar ao software, iluminação, destreza manual, familiaridade com dispositivos móveis/tablet e conhecimento do usuário do serviço para realizar consultas de base tecnológica. Devido a essas considerações, a videoconferência tem um papel limitado e deve ser usada com cuidado [2,17]. Outras limitações observadas são os poucos estudos existentes na literatura correlacionando a TO e o acompanhamento de pacientes

com CO e CCP, tanto no cuidado direto das complicações odontológicas durante o tratamento oncológico quanto pelo agravo causado pelo próprio tratamento do câncer.

As tecnologias como, o uso de aplicativos de celular [18,19], programas baseados na web [20,21–23] e dispositivos conectados à linha telefônica [24,25] para o monitoramento de pacientes com CCP tem se tornado comuns na literatura. Estudos [24,20–23,25] tem mostrado que o monitoramento remoto e/ou o autogerenciamento de sintomas por meio de aplicativos móveis são viáveis para a maioria dos pacientes, com graus satisfatórios de aceitabilidade, satisfação, usabilidade e adesão.

Em programas online como o "*My Journey Ahead*", a maioria dos participantes (70%) visitou o programa mais de uma vez e 61% visualizaram todas as unidades do programa. Os pacientes que aderiram ao programa recomendaram que ter tido acesso a ele no início de sua experiência com o câncer teria sido útil [20]. O aparelho "*Health Buddy*®" teve uma porcentagem mediana de uso de 94,2%, demonstrando uma boa taxa de adesão [24] e um nível de uso entre 75% e 91%. O uso do aplicativo "*mHealth*" reduziu a incerteza e aumentou a aceitação de seu uso, bem como sua adesão. E o aplicativo "*HeNeA*" constatou que a utilidade percebida e a usabilidade contribuíram para a aceitação do usuário e, consequentemente, adesão ao uso [18]. Dessa forma, a partir da manutenção da adesão do paciente às tecnologias remotas, a telessaúde se apresenta como um método promissor para melhorar o autogerenciamento e pode ser utilizada como parte de um programa de monitoramento abrangente [26–28].

Estudos que avaliam a satisfação do usuário as tecnologias remotas de gerenciamento mostraram um índice alto de satisfação com o seu uso. "*Health Buddy*®", "*Oncokompas*", "*HeNeA*" e "*mHealth*" tiveram seu grau de satisfação associados à facilidade de instalação, conteúdo útil, percepção de utilidade, usabilidade, uso pretendido e utilidade. Estudos demonstraram que as tecnologias remotas apresentam um alto nível de satisfação do usuário no monitoramento das condições de saúde [29,30].

O efeito das tecnologias remotas na QV em pacientes com CCP está relacionado à porcentagem usada, bem-estar físico e bem-estar emocional durante o tratamento, o que sugere que o uso de aplicativos de telessaúde resultou em aspectos físicos e emocionais de melhoria de QV [24]. O efeito de tecnologias

remotas na QV parece durar mais entre pacientes com câncer com autoeficácia baixa a moderada, sobreviventes com maior controle pessoal e aqueles com maior conhecimento em saúde [22].

Em pacientes com câncer com autoeficácia baixa a moderada, as tecnologias remotas podem atuar como um incentivo e fornecem as ferramentas para melhorar a QV. Pacientes oncológicos com maior controle pessoal provavelmente se sentem no controle do aplicativo, o que leva a uma melhora precoce na QV A alfabetização em saúde é conhecida por ser um fator importante nas intervenções de eHealth [31] e está positivamente associada à QV [32–34].

No entanto, existem aspectos negativos inerentes ao uso de aplicativos de telessaúde no monitoramento de pacientes com câncer. Aplicativos de telessaúde [35,36] que estabelecem um monitoramento diário dos sintomas por meio de uma resposta de voz interativa ao telefone podem ser considerados desconfortáveis para os pacientes em acompanhamento de longo prazo. Da mesma forma, intervenções exclusivamente baseadas na web [37,38] tendem a ser impraticáveis, devido à necessidade de uma conexão com a internet quando o paciente deseja relatar um sintoma, além de ter que fazer login sempre com seu nome de usuário e senha. Nos sistemas de atendimento por telefone, é necessário melhorar os métodos de comunicação para tornar a interação entre paciente/profissional mais eficaz e melhorar o gerenciamento de sintomas [39-41].

A literatura aponta algumas limitações como estudos que usaram amostras de conveniência, alguns com número modesto de participantes ou avaliadores [18,20–25]; sobrecarga de conteúdo e informação para usuários de tecnologias remotas [24,20,21]; uso em uma única instituição [25,19]; investimento de tempo necessário para completar a aplicação [21]; curto período de acompanhamento [21,19]; falta de avaliação da melhoria do processo de atendimento e disponibilidade em uma única plataforma móvel de tecnologia remota [18]; e a possibilidade dos resultados não refletirem a situação de cada usuário [21]. Apesar das limitações, observa-se a potencialidade do uso de tecnologias remotas de forma viável e aceitável no monitoramento do CCP, necessitando de pesquisa qualitativa com investigação mais profunda baseada em análise longitudinal.

Apesar das limitações, a legislação sobre a TO, no Brasil, vem de um processo de construção que foi acelerado pelo advento da pandemia de COVID-19. A Lei nº 5.081 de 24 de agosto de 1966, que regula o exercício da Odontologia no

Brasil, decorre o registro de que "é vedado ao cirurgião-dentista consultas mediante correspondência, rádio, televisão, ou meios semelhantes". Esse fato trouxe ao exercício da TO um campo de discussões, apesar das benesses observadas durante a pandemia da COVID-19. Em 2020, houve a publicação da Resolução 226/2020, na qual "fica expressamente vedado o exercício da Odontologia a distância, mediado por tecnologias, para fins de consulta, diagnóstico, prescrição e elaboração de plano de tratamento odontológico". Observando-se a discussão sobre os avanços tecnológicos e a ciência da TO, sendo construída internacionalmente e ganhando força e significado após à pandemia, a Resolução 228/2020, publicada em seguida, faz um recorte importante para a aplicação da Odontologia a distância no âmbito do SUS, porém restringindo ao tempo de pandemia [42]. E, no fim do ano de 2022, foi promulgada a Lei 14.510/22, que autoriza e conceitua a prática da telessaúde em todo o território nacional, garantindo o exercício da telessaúde não só ao profissional médico mas também a todo profissional de saúde.

No contexto educacional, evidências crescentes confirmam que o e-learning é tão eficaz quanto os métodos tradicionais de ensino [43,44,45]. A aprendizagem por dispositivo móvel é um subtipo de e-learning, embora não haja um acordo entre os estudiosos sobre sua definição devido à mobilidade tanto da tecnologia quanto da própria aprendizagem, isto é, pode acontecer em qualquer lugar e a qualquer hora [46]. Esta modalidade de ensino também permite que os professores personalizem a instrução com apoio tecnológico e que os alunos autorregulem a sua própria aprendizagem. Além disso, a aprendizagem móvel ajuda os estudantes a desenvolver habilidades tecnológicas e de conversação, encontrar respostas para suas perguntas, desenvolver um senso de colaboração ao permitir o compartilhamento de conhecimento e, assim, alavancar seus resultados de aprendizagem [47]. Durante o período de pandemia, a maioria das tecnologias adotadas para o ensino emergencial remoto em odontologia possuía interfaces de computador e telefone celular, ou uma interface apenas móvel, com o intuito de replicar um cenário de atendimento clínico, dentre eles encontros virtuais entre aprendizes e pacientes representados por atores, simulando a interação clínica, a fim desenvolver habilidades diagnósticas e de definição de planos de tratamento dos estudantes [43]. Dessa forma, o tamanho do efeito em contextos educacionais foi maior para o uso da aprendizagem móvel em locais informais do que em locais formais. Como os dispositivos móveis são inerentemente portáteis, os

pesquisadores observaram a exploração do uso da aprendizagem móvel em contextos além da sala de aula tradicional. Essa disponibilidade quase onipresente torna o uso da aprendizagem móvel em ambientes informais uma alternativa real para a assimilação dos estudantes [48].

Os problemas técnicos relacionados ao cenário educacional se assemelham com os de assistência remota e englobam o conhecimento tecnológico limitado e a falta de treinamento continuado dos docentes, a conexão ruim com a Internet nas universidades, o recurso financeiro insuficiente e as dificuldades para converter alguns tópicos para a versão remota [43]. Existe ainda a necessidade de melhor investigar o tipo de pedagogia usada nas demandas de aprendizagem móvel em estudos futuros, considerando que os dispositivos móveis requerem um método pedagógico adequado para aumentar o desempenho dos estudantes [48]. Além disso, problemas subjetivos atribuídos tanto a docentes quanto a estudantes também foram descritos, como a ansiedade e a incerteza devido ao distanciamento social, desconforto físico e mental, solidão e estresse [49].

O próximo passo, após a conclusão da simulação, das suas funcionalidades será a criação do aplicativo propriamente dito e sua validação. Embora a literatura mostre a validação de várias "ferramentas" para e-saúde [50, 51], não há orientação específica para a validação de "estruturas" de prontidão para e-saúde, que é a preparação de instituições de saúde ou comunidades para a mudança antecipada trazida por programas relacionados às TIC. A "validação" pode ser realizada de várias maneiras. Algumas abordagens envolvem avaliação psicométrica [52] ou validação de face e conteúdo [53]. Outros usam opiniões amplas coletadas por meio de mídias sociais (Facebook e LinkedIn) e autoadministração de uma pesquisa ou entrevistas com uma amostra de usuários [54]. No contexto educacional, ao examinar como validar estruturas de qualidade em e-learning, seis abordagens para validação são identificadas, incluindo revisão da literatura de pesquisa apropriada, realização de pesquisa de levantamento e uso do conhecimento de especialistas na área [55]. No geral, nenhuma abordagem específica e aceita para validação de estruturas relacionadas à e-saúde é explicitamente descrita na literatura. Nesse cenário, a validação é considerada o processo de estabelecer evidências que confirmam que o aplicativo desenvolvido será capaz de atender às necessidades operacionais dos usuários de forma planejada, tanto para os pacientes no telemonitoramento/autogerenciamento oncológico quanto como uma ferramenta de

ensino superior a distância. Dessa forma, uma abordagem de pesquisa para buscar a opinião de especialistas, bem como de usuários que utilizam o aplicativo é considerada apropriada para validação, com a escolha do instrumento de validação mais adequado.

Portanto, estudos apontam que a rápida transição para TO e ensino emergencial remoto durante a pandemia foi uma experiência bem-sucedida, e que pode continuar a ser utilizada. A tecnologia reivindica que as universidades forneçam apoio financeiro e recursos de desenvolvimento profissional, como programas para aprimorar as habilidades pedagógicas dos docentes [56].

O advento de tecnologias de AI aplicada a área da saúde surgem como uma alternativa para aumentar a precisão do diagnóstico precoce do câncer, com melhores resultados do tratamento para o paciente, focando na triagem e detecção do câncer por meio de reconhecimento de imagem com intuíto de reduzir os tempos de diagnóstico [57]. Para prever o comportamento e o prognóstico do câncer, a AI emprega abordagens matemáticas que auxiliam na tomada de decisões ou ações com base no pensamento lógico e autônomo e na adaptabilidade efetiva [58-60]. A literatura apresenta o uso de *computer-assisted detection* (CAD) [61-66], algoritmos de *machine learning* [64,67,68] e análise radiômica [69] para detecção e diagnóstico de tumores malignos com base em imagens radiológicas.

Por outro lado, os oncologistas acham difícil compreender como os modelos de (DL) avaliam os dados e fazem julgamentos, uma vez que o grande número de parâmetros envolvidos dificulta a interpretação dos algoritmos pelos profissionais. Devido à necessidade de preservar as informações do paciente é desafiador obter os dados em quantidades suficientes para ter credibilidade no treinamento e validação em DL. As empresas que lidam com esses dados devem aderir às leis atuais de proteção de dados e privacidade em seus países de origem e nos países de residência dos titulares dos dados. Antes de explorar dados delicados, como dados genéticos, deve-se buscar o consentimento informado dos pacientes. Os pacientes devem ser informados sobre os possíveis usos de seus dados e deve-se garantir que todos se beneficiem deles [70,71].

Antes que a AI seja implementada em ambientes do mundo real, também é necessário definir as obrigações legais em caso de mau funcionamento. Além disso, a maioria dos softwares de AI de ponta funciona em um ambiente de teste de "caixa preta", o que significa que os usuários desconhecem o funcionamento fundamental

do software. O testador apenas conhece a entrada/saída; o raciocínio por trás de chegar a uma determinada conclusão ainda é um mistério. Os médicos frequentemente enfrentam enigmas morais ao fazer previsões sem uma compreensão completa dos processos subjacentes a eles, portanto, é imperativo oferecer maior transparência nos modelos de AI criando técnicas que permitem aos usuários examinar os detalhes dos dados de entrada que afetaram o resultado mais perto da verdade [70-72].

E à medida que mais tecnologias de AI são criadas com potencial para aplicação clínica, é fundamental abordar as questões éticas, médico-legais e regulatórias associadas. Há muitas questões sem resposta na área da ética. Em que situações os médicos devem dizer a seus pacientes que estão usando técnicas de AI em seus exames clínicos? Essa questão pode ser crucial em cenários em que a AI funciona como uma "caixa preta", na qual os médicos agem com base na saída de uma ferramenta de AI sem saber como o algoritmo chegou a essa conclusão. Quando uma tecnologia de AI não detecta um câncer, quem é o responsável? Quanto do processo deve estar sob controle humano? Os sistemas DL CAD são os únicos responsáveis pelas decisões finais de diagnóstico? Quem é responsável pelas más decisões de DL? Os radiologistas serão tendenciosos com o resultado da assistência da AI? Quais são as percepções das pessoas sobre as ferramentas de decisão de DL? Os algoritmos DL CAD podem descrever corretamente seu processo de pensamento? É claro que deve haver discussão sobre esses vieses algorítmicos, que também levantam preocupações éticas, antes que os modelos DL sejam amplamente utilizados em ambientes clínicos reais [73,74].

Embora a AI seja uma tecnologia promissora, com potencial considerável na área de saúde, em especial no processo de diagnósticos, sua aplicação clínica generalizada ainda carece de viabilidade. Essa viabilidade não se traduz numa ampla aplicação clínica, sendo usada de forma pontual, principalmente em áreas de pesquisa.

Aspectos como, tamanho e acesso ao banco de dados para treinamento dos modelos de AI, questões éticas e legais, especificidade/sensibilidade dos algorítimos somente para alguns tipos de câncer, falta de compreensão do raciocínio do processo de decisão do modelo de AI, necessidade de grande quantidade de dados, a não utilização de dados sociais e culturais para melhorar modelos preditivos baseados em AI e a falta de cooperação entre pesquisadores em medicina e ciência

da computação necessitam serem solucionados para uma maior efetividade dos modelos baseados em AI.

Esse trabalho mostra que a implantação da TO regionalizada pode ser utilizada em áreas como monitoramento de pacientes oncológicos, podendo ser expandido para outras áreas da odontologia como no caso da estomatologia/patologia bucal, nas análises de lesões bucais em populações que carecem de um especialista, de forma remota. Isto gera diminuição de custos, otimização de consultas, celeridade e continuidade dos serviços de atendimento, segurança ao paciente, diminuição dos casos graves de câncer oral, manejo no uso de medicamentos, autogestão do usuário, a monitorização remota de sintomas e resposta ao tratamento, entre outros.

No contexto pós-pandêmico que o mundo se encontra, a TO pode ser de grande utilidade não só no controle de disseminação de agentes infecciosos, mas também no acesso à saúde a grupos populacionais específicos como as populações ribeirinhas, populações de zona rurais isoladas, populações indígenas, pacientes portadores de deficiência com graves dificuldade de locomoção e populações acometidas de desastes naturais. É necessário a criação de núcleos de telessaúde regionalizados que garantam acesso a especialistas como radiologistas orais, estomatologistas, patologistas bucais, cirurgiões bucomaxilofaciais de forma que casos clínicos iniciais possam ser discutidos e, senão resolvidos no nível de atenção primário, possa ser encaminhados, via sistema de regulação específico, para atendimento no nível de atenção secundário e/ou de forma mais célere possível de forma a evitar a progressão de um caso suspeito de câncer oral.

As revisões realizadas nesse trabalho corroboram com a literatura [75-78] quanto à viabilidade da TO, mas ainda com ressalvas a sua generalização. A pandemia de COVID-19 promoveu o aceleramento da massificação da telessaúde, entretanto ainda carece de meios governamentais e privados para se tornar generalizado. Questões como o acesso à internet, familiaridade com a tecnologia pelos usuários, necessidade de softwares compatíveis, e um sistema integrado de saúde pública e privada precisam ser resolvidas antes da generalização do uso.

5.2 CONCLUSÕES

A partir desse trabalho realizado fica evidente que a assistência a saúde mediada por tecnologias remotas apresenta viabilidade, tanto durante o período de pandemia recente como agora no pós-pandemia. Nas revisões realizadas observou-se que 78% dos pacientes atualmente preferem a TO; 92% dos pacientes recomendariam o uso da videoconsulta a outros pacientes. A continuidade do atendimento odontológico, a redução de visitas de pacientes ao hospital, a redução do risco de infecção pelo coronavírus e a limitação de consultas presenciais para proteger os profissionais de saúde são benefícios que reforçam o uso da TO pelas instituições de saúde. Embora tenha sido observado heterogeneidade quanto à tecnologia utilizada, o monitoramento remoto e/ou autogerenciamento dos sintomas por meio de aplicativos móveis foi viável para a maioria dos pacientes, com graus satisfatórios de aceitabilidade, satisfação, usabilidade e adesão. Cabe salientar que as várias abordagens de modelos de AI são promissoras em termos de especificidade, sensibilidade e precisão diagnóstica na detecção e diagnóstico de tumores malignos.

O monitoramento realizado por meio de aplicativos de celular, programas baseados na web e dispositivos conectados à linha telefônica apresentam-se como uma alternativa de apoio à educação e cuidado dos pacientes durante o tratamento do CCP, demonstrando alguma melhora na QV associada a saúde, disponibilidade e adesão ao uso. E a interação dessas tecnologias remotas com a AI parecem ser viáveis e precisas quando utilizadas na detecção e diagnóstico de tumores malignos com o uso de sistemas CAD, algoritmos de ML e análise radiômica quando comparado ao modelo tradicional.

A TO, como tecnologia remota para monitoramento de pacientes com CO e CPP, é bem aceita por pacientes e profissionais, embora não de forma consensual. Dessa maneira, a TO gerenciada por tecnologias remotas e associada a AI apresenta muitos desafios, como a falta de aceitação da TO por parte dos cirurgiões-dentistas; receio de fazer um diagnóstico impreciso; preocupações com aumento de custos, despesas e infraestrutura necessária; reembolso financeiro insuficiente e orientações inadequadas; ansiedade tecnológica, isolamento, sentimentos de descaso e medos por parte dos pacientes; dificuldades quanto ao

atraso no tratamento oncológico; dificuldades de acesso a serviços de apoio durante a pandemia de COVID-19; necessidade de uma interface mais amigável; avaliação adequada da experiência do usuário; aplicabilidade concreta de tecnologias de telessaúde para monitoramento de pacientes com CCP; melhor desempenho somente em alguns tipos específicos de tumores, como câncer de mama, câncer de próstata e nódulos de tireoide; limitações quanto à generalização para todos os tipos de câncer; e melhor desempenho dos algoritmos ML quando comparados aos métodos DL.

Portanto, estudos com foco na TO, padronizados e longitudinais, com envolvimento multicêntrico e multidisciplinar, devem ser realizados usando tecnologias remotas associado a algoritmos de AI para gerenciar o monitoramento odontológico de CO e de CPP, além da possibilidade do uso na detecção de lesões malignas em diferentes modalidades de imagem, usando conjuntos de dados maiores. Essas perspectivas permitirão consolidar os benefícios do uso de tecnologias remotas de monitoramento como alternativa viável para o acompanhamento de pacientes oncológicos e uma melhor compreensão do uso da AI na prática clínica oncológica.

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CAPÍTULO 6 – PRESS RELEASE

A Teleodontologia (TO) é uma modalidade da odontologia que viabiliza o atendimento odontológico à distância, por meio de tecnologias digitais. Essa já é uma prática muito comum e regulamentada em outros países, e foi impulsionada no Brasil devido à pandemia de COVID-19. Devido a pandemia, houve à interrupção da prestação de cuidados odontológicos a todos os pacientes em tratamento oncológico. A TO atua para evitar a interrupção do atendimento através do fornecimento de auxílio aos pacientes que fazem a rádio e/ou quimioterapia e motivação com ênfase as medidas de higiene oral usando o telefone e, quando possível, vídeo-chamadas.

É cada dia mais comum o uso tecnologias como, o uso de aplicativos móveis de celular, páginas na internet e dispositivos conectados à linha telefônica para o monitoramento de pacientes com câncer com graus de aceitação e satisfação do uso. Aliado a isso, o surgimento da AI aplicada a área da saúde desponta como uma alternativa para aumentar o diagnóstico precoce do câncer, com melhores resultados para o paciente, focando na detecção do câncer por meio do uso de exame de imagem com para reduzir o tempo de diagnóstico.

O uso das tecnologias de forma remota em saúde, em especial na odontologia, possui impacto na vida moderna atualmente, pois permite a continuidade do acompanhamento da saúde bucal, redução de deslocamentos para atendimento de pacientes no hospital, redução do risco de infecção pelo coronavírus entre outros. Embora haja desafios como, receio de fazer um diagnóstico impreciso, preocupações com aumento de custos, despesas e infraestrutura necessária, necessidade de uma interface mais amigável, limitações quanto à generalização para detecção de todos os tipos de câncer, a TO gerenciada por tecnologias remotas e associada a IA podem gerar muitos benefícios no futuro e promover melhorias reais a QV durante e após tratamento oncológico.