

## Clinical decision support system, a potential solution for diagnostic accuracy improvement in oral squamous cell carcinoma: A systematic review

Hamideh Ehtesham MSc<sup>1</sup>, Reza Safdari PhD<sup>2</sup>, Arash Mansourian DDS, MSc<sup>3</sup>,  
Shahram Tahmasebian PhD<sup>4</sup>, Niloofar Mohammadzadeh PhD<sup>5</sup>,  
Marjan Ghazisaeedi PhD<sup>5</sup>, Azadeh Bashiri MSc<sup>1</sup>

### Review Article

#### Abstract

**BACKGROUND AND AIM:** Oral squamous cell carcinoma (OSCC) is a rapidly progressive disease and despite the progress in the treatment of cancer, remains a life-threatening illness with a poor prognosis. Diagnostic techniques of the oral cavity are not painful, non-invasive, simple and inexpensive methods. Clinical decision support systems (CDSSs) are the most important diagnostic technologies used to help health professionals to analyze patients' data and make decisions. This paper, by studying CDSS applications in the process of providing care for the cancer patients, has looked into the CDSS potentials in OSCC diagnosis.

**METHODS:** We retrieved relevant articles indexed in MEDLINE/PubMed database using high-quality keywords. First, the title and then the abstract of the related articles were reviewed in the step of screening. Only research articles which had designed clinical decision support system in different stages of providing care for the cancer patient were retained in this study according to the input criteria.

**RESULTS:** Various studies have been conducted about the important roles of CDSS in health processes related to different types of cancer. According to the aim of studies, we categorized them into several groups including treatment, diagnosis, risk assessment, screening, and survival estimation.

**CONCLUSION:** Successful experiences in the field of CDSS applications in different types of cancer have indicated that machine learning methods have a high potential to manage the data and diagnostic improvement in OSCC intelligently and accurately.

**KEYWORDS:** Squamous Cell Carcinoma; Clinical Decision Support System; Neoplasm; Dental Informatics

**Citation:** Ehtesham H, Safdari R, Mansourian A, Tahmasebian S, Mohammadzadeh N, Ghazisaeedi M, et al. **Clinical decision support system, a potential solution for diagnostic accuracy improvement in oral squamous cell carcinoma: A systematic review.** *J Oral Health Oral Epidemiol* 2017; 6(4): 187-95.

Oral cavity cancer refers to all malignancies of the lips, mouth and neck, among which oral squamous cell carcinoma (OSCC) is the most common one.<sup>1,2</sup> Etiology and biological behavior studies of OSCC have suggested that this carcinoma develops a more

aggressive behavior with poor prognosis.<sup>3,4</sup>

In response to the need for early detection of OSCC, several diagnostic techniques have been developed over the years, mostly including vital staining, light-based detection systems, histological techniques, cytological techniques, molecular analyses and imaging

1- PhD Candidate, Department of Health Information Management, School of Allied Medical Sciences, Tehran University of Medical Sciences, Tehran, Iran

2- Professor, Department of Health Information Management, School of Allied Medical Sciences, Tehran University of Medical Sciences, Tehran, Iran

3- Associate Professor, Department of Oral Medicine and Dental Research Center, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran

4- Assistant Professor, School of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran

5- Assistant Professor, Department of Health Information Management, School of Allied Medical Sciences, Tehran University of Medical Sciences, Tehran, Iran

Correspondence to: Reza Safdari PhD and Arash Mansourian DDS, MSc

Email: rsafdari@tums.ac.ir, amansourian@tums.ac.ir

techniques.<sup>5,6</sup> One of the most considerable improvements in the healthcare area is a trend to the non-invasive interventions in the diagnosis and treatment of diseases.

In recent years, numerous studies have been conducted to identify and assess the diagnostic biomarkers for OSCC. Identification of reliable biological tumor markers showed high sensitivity, efficiency and specificity for oral cancer and can be an additional tool for diagnosis, prognosis and treatment monitoring of patients with cancer.<sup>7</sup>

Also, use of the computers to assist health professionals in their activities has become popular in recent decades. The first efforts focused on the development of diagnostic systems. Clinical decision support systems (CDSSs) are the most important diagnostic technologies used to help health professionals to analyze patient data and make decisions.<sup>8</sup>

The advent of high information technology and dental devices has produced vast amounts of data. Moreover, the use of data mining algorithms and artificial intelligence techniques in dental informatics has a great potential to manage new big data. However, few efforts have been made to apply these techniques and relatively little research has been conducted to retrieve meaningful information from dental data. Some studies have used k-means clustering methods to establish normative data on tooth size<sup>9</sup> in order to categorize the patients with facial asymmetry into the groups with different characteristics.<sup>10</sup> Detection of oral cancer by applying k-means clustering and principal component analyses was carried out by the spectra obtained from autofluorescence spectroscopy.<sup>11</sup>

The use of expert systems also has been associated with successful experiences in dentistry. For example, an expert system has helped decision making and treatment of the most common periodontal conditions.<sup>12</sup> Another expert system has used neural artificial intelligence to test the accuracy of periodontal disease risk assessment.<sup>13</sup>

Moreover, another expert system has determined the diagnosis, disease severity and the treatment methods in periodontal diseases based on the patient clinical data and radiographic findings.<sup>14</sup>

The appearance of CDSS in dentistry has addressed the several major areas of dental practice. Different types of knowledge representation and different modalities have been used in its development. A prediction system was developed in orthodontics where extraction/non-extraction decisions are very important. This system has been successfully optimized to obtain the concise representation of the expertise knowledge elements with prediction accuracy.<sup>15</sup> A triage tool was designed and successfully evaluated to determine the patient's examination waiting time by describing their clinical symptoms in the dental care unit.<sup>16</sup> A study was conducted with the objective of developing a decision support system for predicting the degree of color change after in-office tooth whitening by using colorimetric values. The patients' post-treatment color was largely close to the system prediction.<sup>17</sup>

A comprehensive review of the literature on decision support applications in dentistry, grouped these systems into seven subareas of dentistry: dental emergencies and trauma, orofacial pain, oral medicine, oral radiology, orthodontics, pulpal diagnosis, and restorative dentistry.<sup>18</sup>

CDSSs have a great potential for providing the opportunities to improve patient care in various fields of oral medicine especially in oral cancer, through managing a large amount of data intelligently.

The present study aims to review the literature on the CDSS applications in cancer with special attention to oral cancer. Therefore, key questions in this study include: 1- What are the CDSS applications in the process of providing care for the cancer patient? 2- What applications have been used in oral cancer? 3- Have been CDSS applications used in OSCC?

A description with details of the CDSS

applications in health processes related to different types of cancer provides an appropriate model for highlighting their potentials for diagnostic accuracy improvement in OSCC.

## Methods

This study was a systematic review to identify articles published in PubMed and focusing on CDSS applications in cancer. We searched the database in September 2016 with the following strategy: ("Neoplasms"[MeSH]) AND "Decision Support Systems, Clinical"[MeSH] AND Humans [MeSH] AND English [lang]) Filters: Humans; English.

After the identification step, we screened the titles and abstracts of the related articles according to the inclusion/exclusion criteria. Inclusion criteria included only original articles, designed and used clinical decision support system in different stages of providing care for the cancer patients. No date restriction was applied to the search. Due to the limitations of searching database alone and in order to avoid missing related articles, we focused on article citations and before-and-after studies. Studies were excluded where they were not relevant to the key questions. The search was limited to journal articles written in the English language. Letters, reviews and conference

proceedings also were excluded.

After screening the titles and abstracts of potential articles, remaining studies were subjected to the screening of their main content, which in turn, their full-texts were reviewed. Figure 1 shows the flow of the article selection procedure.

Data extraction and validity assessment were performed in two steps. First, a checklist was developed as an assessment tool with the aim of answering the key questions. Intended variables included references, objective, cancer type and result. Details from each article were extracted by two independent reviewers. In the second step and in order to have a systemic investigation, the variables collected in the data extraction form were classified into separate groups.

## Results

A total of 414 potentially relevant titles, abstracts, and articles were found in MEDLINE/PubMed search. Non-pertinent papers were excluded according to inclusion and exclusion criteria after screening the titles and abstracts. We reviewed the full-texts of the remaining 82 articles. Finally, 17 articles met the inclusion criteria and considered as the final samples. Table 1 indicates the variable extracted from articles.

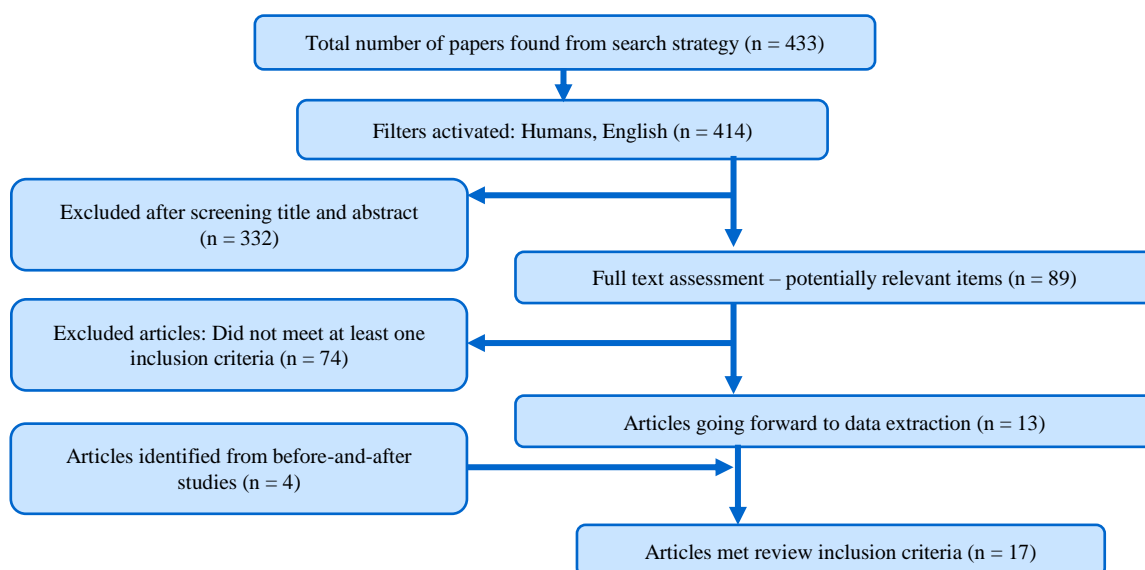


Figure 1. Article selection procedure

**Table 1.** Characteristics of included studies

Reference	Objective	Cancer type	Result
Abernethy et al. <sup>19</sup>	Educates clinical decision makers and healthcare professionals about the burden of cancer pain in their individual populations	ALL	Leads to improved pain control with modest increases in resource use
Finlayson et al. <sup>20</sup>	Providing an analytical engine and user interface that enables physicians to gain clinical insights by rapidly identifying and analyzing cohorts of patients similar to their own	Melanoma	The MRLU is an important component in building an RLS for data-driven precision medicine in melanoma treatment that could be generalized to other clinical disorders
Mi et al. <sup>21</sup>	To select predictive features from clinical and PET-based features, in order to provide doctors with informative factors so as to anticipate the outcome of the patient treatment	ALL	Addition of prior knowledge improves the robustness and accelerates the convergence
Cakir and Demirel <sup>22</sup>	To help to oncology doctor for the suggestion of application of the treatment methods about breast cancer patients	Breast cancer	Data mining approach can be a useful tool for medical applications particularly at the treatment decision step
Bury et al. <sup>23</sup>	To assist with dosage adjustments during maintenance therapy for childhood ALL	Lymphoblastic Leukaemia	Improvement in time taken to manage each case; accuracy of dosage calculations
Gerbert et al. <sup>24</sup>	To determine whether decision support software can help primary care physicians proficiently triage lesions suggestive of basal cell and squamous cell carcinoma	Skin cancer	Use of decision support software could improve primary care physicians' triage decisions for lesions suggestive of non-melanoma skin cancer, and potentially reduce morbidity and health care costs
Emery et al. <sup>25</sup>	To evaluate the effect of an assessment strategy using the computer decision support system (the GRAIDS software), on the management of familial cancer risk	Familial breast or colorectal cancer	Improved practitioner confidence and had no adverse psychological effects in patients
Ozanne et al. <sup>26</sup>	Provides automated risk assessment and personalized decision support designed for collaborative use between patients and clinicians	Breast cancer	The ability to integrate risk assessment and decision support in real time will allow for informed, value-driven, and patient-centered breast cancer prevention decisions
Javan Amoli et al. <sup>27</sup>	Electronic risk assessment system as an appropriate tool for the prevention of cancer	ALL	Electronic pathways have been applied for clinical and genetic decision support, workflow management, update recommendation and resource estimates
Shelton et al. <sup>28</sup>	Implemented guidelines seeking to reduce PSA-based screening for prostate cancer in men aged 75 years and older	Prostate cancer	With this simple intervention, evidence-based guidelines were brought to bear at the point of care, precisely for the patients and providers for whom they were most helpful, resulting in more appropriate use of medical resources
Hills et al. <sup>29</sup>	Improving guideline-consistent cervical cancer screening practices in an urban safety net clinic	Cervical cancer	Patients screened according to guidelines nearly doubled while the number of underscreened patients was reduced by nearly half. Similarly, there was a threefold decrease in patients screened more frequently than recommended
Maserat et al. <sup>30</sup>	To detail engineering of information requirements and workflow design of CDSS for a colorectal cancer screening program	Colorectal cancer	A CDSS facilitates complex decision making for screening and has key roles in designing optimal interactions between colonoscopy, pathology and laboratory departments
Lundin et al. <sup>31</sup>	To evaluate the accuracy of an Internet-based method for survival estimation in breast cancer	Breast cancer	A web-based case-match system can generate survival curves for user-defined prognostic factor combinations and identify patients with a varying risk for breast cancer recurrence

**Table 1.** Characteristics of included studies (continue)

Reference	Objective	Cancer type	Result
Sidiropoulos et al. <sup>32</sup>	Supporting rare cancers decision making operates on a GPU and adjusting its design in real-time based on user-defined clinical questions in contrast to standard CPU implementations	Brain cancer	Enables real-time, optimal design of a CDSS for any user-defined clinical question for improving diagnostic assessments, prognostic relevance and concordance rates for rare cancers in clinical practice
Exarchos et al. <sup>33</sup>	To identify the factors that dictate OSCC progression and subsequently predict potential relapses (local or metastatic) of the disease	Oral squamous cell carcinoma	The discrimination potential of each source of data is initially explored separately, and afterward, the individual predictions are combined to yield a consensus decision achieving complete discrimination between patients with and without a disease relapse
Nguyen et al. <sup>34</sup>	To classify automatically lung TNM cancer stages from free-text pathology reports using symbolic rule-based classification	Lung tumor	It was verified that the symbolic rule-based approach using SNOMED CT can be used for the extraction of key lung cancer characteristics from free-text reports
Nguyen et al. <sup>35</sup>	Development of a Web-enabled relational database integrated with decision-making tools for teaching flow cytometric diagnosis of hematologic neoplasms	Hematologic neoplasm	This database shows significant improvement in diagnostic accuracy over our previous database prototype

ALL: Acute lymphoblastic leukemia; MRLU: Melanoma rapid learning utility; RLS: Rapid learning system; PET: Positron emission tomography; PSA: Prostate-specific antigen; CDSSs: Clinical decision support systems; GPU: Graphics Processing Unit; CPU: Central processing unit; OSCC: Oral squamous cell carcinoma; TNM: Tumor-node-metastasis; SNOMED CT: Systematized nomenclature of medicine-clinical term

In order to answer the key questions, we categorized the articles according to CDSS applications in the different stages of providing care for the cancer patients, including diagnosis, treatment, risk assessment, screening and survival estimation.

CDSSs play an important role in different stages of cancer diagnosis and treatment. For example, some of these include a challenging decision making on chemotherapy protocols for a patient,<sup>36</sup> supported the nurses' decision-making process about patients' needs and preparation of individual care plans.<sup>37</sup> Another example of CDSS application is to help with the diagnosis within a gastroenterology room during real endoscopy examinations with human-computer interaction (HCI) support methodologies in order to identify interaction opportunities,<sup>38</sup> and precise selection of meningioma brain histopathological image classification.<sup>39</sup> Also, it is used as a practical tool to improve the selection of protocols for monitoring, diagnosing, and treating cervical cancer in women and the patient-specific follow-up decision making for them.<sup>40</sup> Some

decision support systems have examined drug interactions of various diseases and may lead to undesirable and sometimes life-threatening reactions.<sup>41</sup>

Furthermore, cancer screening programs have been run in different countries as a primary preventive measures in order to reduce damage and focus on the high-risk groups of cancer.<sup>7</sup> In the screening process and to manage the cases with a positive test, especially for the patients at risk of developing cancer, presenting the report of the follow-up referral with the aim of providing therapeutic suggestions can be very effective. CDSSs have an important role in this context and upgrade the quality of the screening programs significantly. Moreover, the time saving of 1 minute and 39 seconds per patient consultation for providers has been calculated.<sup>42</sup>

Few studies have examined the application of machine learning methods in OSCC. Only a multiparametric decision support system formulated for the prediction of OSCC recurrence. In this system, collected different type of data have included



clinical data, imaging and gene expression data in order to identify the factors that have potential involvement in OSCC progression and subsequently predict the possibility of a recurrence of the disease.<sup>43</sup> Table 2 shows some of the different applications of CDSS in the stages of cancer.

### Discussion

The advent of information technology in the field of medicine, and in particular the application of artificial intelligence, has led to significant progress in the data management especially in chronic diseases such as cancer. Discovering the patterns and relationships between them from the multiple and complex data sets have facilitated the effective prediction of future outcomes of cancer.<sup>44</sup> In recent years, many studies have used molecular, clinical or population-based data to predict cancer susceptibility,<sup>45</sup> recurrence<sup>43</sup> and survival.<sup>46,47</sup>

Due to the nature of medical data, the success of any intelligent system largely depends on the input data optimality; therefore, using data mining approaches are essential in order to reduce the data dimension, optimal choice and Increase in accuracy.<sup>48</sup>

Understanding of tumorigenesis can have a positive effect on the diagnosis and treatment process and also designing the more effective CDSSs. Different studies indicated that the following stages are required for cancer to form: 1- Acquisition of autonomous proliferative signaling, 2- Inhibition of growth inhibitory signals, 3- Evasion of programmed cell death, 4- Immortalization, 5- Acquisition of a nutrient blood supply (angiogenesis) and 6- Acquisition of the ability to invade tissue.<sup>44,49,50</sup>

Although significant progress has been made in the treatment of cancer, survival rate remains unchanged and oral cancer remains a life-threatening illness with a poor prognosis.<sup>51</sup>

OSCC is a rapidly progressive disease, although it can be a slower process by using several mechanisms, including defective antigen presentation, interference with tumor-T cell interaction and production of

immunosuppressive factors.<sup>52</sup>

Various studies have been conducted about the potentials and limitations of microarrays for the prediction of OSCC outcome, based on gene expression signatures.<sup>53,54</sup> The bioinformatics method that can be used to distinguish OSCC and normal tissues is gene ontology (GO). GO analysis was used to investigate the critical genes in the progression of OSCC and protein-protein interaction (PPI) networks. Moreover, pathway enrichment analysis was performed to estimate the significant pathways.<sup>55</sup> Studies that examine the impact of proteins on development and metastasis of OSCC through regulation of transcriptional responses, differentiation, angiogenesis, proliferation, and apoptotic programs can help researchers identify crucial targets for the prevention and treatment of OSCC.<sup>56</sup>

The importance of early diagnosis, the prognosis of cancer type, classifying cancer patients into high or low-risk groups, also an improvement in screening uptake by a combination of risk factors including genetic, environmental and behavioral risk factors in primary care led to an interest in the use of information technology and artificial intelligence in this area.<sup>57</sup>

Various surveys on the system development process have indicated the significant evolutions toward an effective improvement with regards to the patient, attention to organizational and economic issues and use of standard models for knowledge representation.<sup>58</sup> Dentists positive attitudes at the outset of a system change can help organizational administrators with the adoption of evidence-based dentistry tools such as a CDSS system.<sup>59</sup>

Efficiency and usability in CDSSs have a significant impact on users' adoption,<sup>60</sup> but designing a system with a multitude of warnings and suggestions and alarms is misleading and ambiguous.<sup>61</sup> Therefore, special attention has to be paid to these points to design a convenient and functional system. Obviously, artificial intelligence

analysis of health data and clinical decision support system must be employed along with clinicians.<sup>62,63</sup> Improving the capabilities of the CDSS and presenting it as an intelligent web service and providing access to dentists, as well as medical researchers, is an effective step in managing new and tracking past patients.

### Conclusion

With the advent of information technologies in the field of medicine, especially computer-based decision aids with embedded algorithms, there have been significant developments in the diagnosis and treatment of diseases.

Clinical decision support system can have an effective role in classifying the patients with OSCC into the higher/lower risk of reoccurrence groups and determine the optimal treatment protocols in a cost-effective manner at the point of caregiver. Furthermore, the significant performance of

the CDSS in improving the accuracy of early detection can play a vital role in reducing invasive treatments.

The trend of diagnostic techniques of the oral cavity towards non-invasive methods and identification of reliable biological tumor markers for OSCC produces a large amount of data. CDSS can manage data intelligently and improve in diagnostic accuracy

Obviously, several studies can be programmed on the application of the CDSS in susceptibility and survivability prediction in OSCC patient.

### Conflict of Interests

Authors have no conflict of interest.

### Acknowledgments

We would like to thank the library staffs of Tehran University of Medical Sciences, Iran, for their sincere cooperation and contribution to get results via searching the articles.

### References

1. Krishna Rao SV, Mejia G, Roberts-Thomson K, Logan R. Epidemiology of oral cancer in Asia in the past decade--an update (2000-2012). *Asian Pac J Cancer Prev* 2013; 14(10): 5567-77.
2. Sahebamee M, Mansourian A, Etemad-Moghadam S, Shamshiri AR, Derakhshan S. Conventional versus Papanicolaou-stained cytobrush biopsy in the diagnosis of oral squamous cell carcinoma. *Oral Health Dent Manag* 2014; 13(3): 619-22.
3. Durr ML, van Zante A, Li D, Kezirian EJ, Wang SJ. Oral tongue squamous cell carcinoma in never-smokers: Analysis of clinicopathologic characteristics and survival. *Otolaryngol Head Neck Surg* 2013; 149(1): 89-96.
4. Soudry E, Preis M, Hod R, Hamzany Y, Hadar T, Bahar G, et al. Squamous cell carcinoma of the oral tongue in patients younger than 30 years: Clinicopathologic features and outcome. *Clin Otolaryngol* 2010; 35(4): 307-12.
5. Carreras-Torras C, Gay-Escoda C. Techniques for early diagnosis of oral squamous cell carcinoma: Systematic review. *Med Oral Patol Oral Cir Bucal* 2015; 20(3): e305-e315.
6. Cheng YS, Rees T, Wright J. Updates regarding diagnostic adjuncts for oral squamous cell carcinoma. *Tex Dent J* 2015; 132(8): 538-49.
7. Tian X, Chen Z, Shi S, Wang X, Wang W, Li N, et al. Clinical diagnostic implications of body fluid MiRNA in oral squamous cell carcinoma: A meta-analysis. *Medicine (Baltimore)* 2015; 94(37): e1324.
8. Mendonca EA. Clinical decision support systems: Perspectives in dentistry. *J Dent Educ* 2004; 68(6): 589-97.
9. Lee SJ, Lee S, Lim J, Ahn SJ, Kim TW. Cluster analysis of tooth size in subjects with normal occlusion. *Am J Orthod Dentofacial Orthop* 2007; 132(6): 796-800.
10. Hwang HS, Youn IS, Lee KH, Lim HJ. Classification of facial asymmetry by cluster analysis. *Am J Orthod Dentofacial Orthop* 2007; 132(3): 279-6.
11. de Veld DC, Skurichina M, Witjes MJ, Duin RP, Sterenborg DJ, Star WM, et al. Autofluorescence characteristics of healthy oral mucosa at different anatomical sites. *Lasers Surg Med* 2003; 32(5): 367-76.
12. Saudi H. A periodontal expert system as an aid in periodontal treatment planning. *Egypt Dent J* 2002; 48: 1087.
13. Shankarapillai R, Mathur K, Nair MA, Rai N, Mathur A. Periodontitis risk assessment using two artificial neural networks-a pilot study. *International Journal of Dental Clinics* 2010; 2(4): 36-40.
14. Allahverdi N, Akcan T. A Fuzzy Expert System design for diagnosis of periodontal dental disease. *Proceedings of the*

- 5<sup>th</sup> International Conference on Application of Information and Communication Technologies (AICT); 2011 Oct 12-14; Baku, Azerbaijan.
15. Yagi M, Ohno H, Takada K. Decision-making system for orthodontic treatment planning based on direct implementation of expertise knowledge. *Conf Proc IEEE Eng Med Biol Soc* 2010; 2010: 2894-7.
  16. Pegon-Machat E, Decerle N, Tubert-Jeannin S. Development and evaluation of a triage tool for patients in a dental emergency unit. *Sante Publique* 2015; 27(1): 79-88. [In French].
  17. Thanathornwong B, Suebnukarn S, Ouivirach K. Decision support system for predicting color change after tooth whitening. *Comput Methods Programs Biomed* 2016; 125: 88-93.
  18. Welch BM, Kawamoto K. Clinical decision support for genetically guided personalized medicine: a systematic review. *J Am Med Inform Assoc* 2013; 20(2): 388-400.
  19. Abernethy AP, Samsa GP, Matchar DB. A clinical decision and economic analysis model of cancer pain management. *Am J Manag Care* 2003; 9(10): 651-64.
  20. Finlayson SG, Levy M, Reddy S, Rubin DL. Toward rapid learning in cancer treatment selection: An analytical engine for practice-based clinical data. *J Biomed Inform* 2016; 60: 104-13.
  21. Mi H, Petitjean C, Dubray B, Vera P, Ruan S. Robust feature selection to predict tumor treatment outcome. *Artif Intell Med* 2015; 64(3): 195-204.
  22. Cakir A, Demirel B. A software tool for determination of breast cancer treatment methods using data mining approach. *J Med Syst* 2011; 35(6): 1503-11.
  23. Bury J, Hurt C, Roy A, Bradburn M, Cross S, Fox J, et al. A quantitative and qualitative evaluation of LISA, a decision support system for chemotherapy dosing in childhood acute lymphoblastic leukaemia. *Stud Health Technol Inform* 2004; 107(Pt 1): 197-201.
  24. Gerbert B, Bronstone A, Maurer T, Hofmann R, Berger T. Decision support software to help primary care physicians triage skin cancer: A pilot study. *Arch Dermatol* 2000; 136(2): 187-92.
  25. Emery J, Morris H, Goodchild R, Fanshawe T, Prevost AT, Bobrow M, et al. The GRAIDS Trial: A cluster randomised controlled trial of computer decision support for the management of familial cancer risk in primary care. *Br J Cancer* 2007; 97(4): 486-93.
  26. Ozanne EM, Howe R, Omer Z, Esserman LJ. Development of a personalized decision aid for breast cancer risk reduction and management. *BMC Med Inform Decis Mak* 2014; 14: 4.
  27. Javan Amoli AH, Maserat E, Safdari R, Zali MR. Electronic Risk Assessment System as an Appropriate Tool for the Prevention of Cancer: A Qualitative Study. *Asian Pac J Cancer Prev* 2015; 16(18): 8595-8.
  28. Shelton JB, Ochotorena L, Bennett C, Shekelle P, Kwan L, Skolarus T, et al. Reducing PSA-based prostate cancer screening in men aged 75 years and older with the use of highly specific computerized clinical decision support. *J Gen Intern Med* 2015; 30(8): 1133-9.
  29. Hills RL, Kulbok PA, Clark M. Evaluating a quality improvement program for cervical cancer screening at an urban safety net clinic. *Health Promot Pract* 2015; 16(5): 631-41.
  30. Maserat E, Seied Farajollah SS, Safdari R, Ghazisaeedi M, Aghdaei HA, Zali MR. Information engineering and workflow design in a clinical decision support system for colorectal cancer screening in Iran. *Asian Pac J Cancer Prev* 2015; 16(15): 6605-8.
  31. Lundin J, Lundin M, Isola J, Joensuu H. Evaluation of a web-based system for survival estimation in breast cancer. *Stud Health Technol Inform* 2003; 95: 788-93.
  32. Sidiropoulos K, Glotsos D, Kostopoulos S, Ravazoula P, Kalatzis I, Cavouras D, et al. Real time decision support system for diagnosis of rare cancers, trained in parallel, on a graphics processing unit. *Comput Biol Med* 2012; 42(4): 376-86.
  33. Exarchos KP, Goletsis Y, Fotiadis DI. A multiscale and multiparametric approach for modeling the progression of oral cancer. *BMC Med Inform Decis Mak* 2012; 12: 136.
  34. Nguyen AN, Lawley MJ, Hansen DP, Bowman RV, Clarke BE, Duhig EE, et al. Symbolic rule-based classification of lung cancer stages from free-text pathology reports. *J Am Med Inform Assoc* 2010; 17(4): 440-5.
  35. Nguyen AN, De J, Nguyen J, Padula A, Qu Z. A teaching database for diagnosis of hematologic neoplasms using immunophenotyping by flow cytometry. *Arch Pathol Lab Med* 2008; 132(5): 829-37.
  36. Righi LV. Oncotherapy: A system for requesting chemotherapy protocols. *Stud Health Technol Inform* 2015; 216: 1121.
  37. Yilmaz AA, Ozdemir L. Development and implementation of the clinical decision support system for patients with cancer and nurses' experiences regarding the system. *Int J Nurs Knowl* 2017; 28(1): 4-12.
  38. Abrantes D, Pimentel-Nunes P, Dinis-Ribeiro M, Coimbra M. Identifying technology interaction opportunities within a gastroenterology exam room. *Stud Health Technol Inform* 2015; 210: 652-6.
  39. Al-Kadi OS. A multiresolution clinical decision support system based on fractal model design for classification of histological brain tumours. *Comput Med Imaging Graph* 2015; 41: 67-79.
  40. Bountris P, Haritou M, Pouliakis A, Margari N, Kyrgiou M, Spathis A, et al. An intelligent clinical decision support



- system for patient-specific predictions to improve cervical intraepithelial neoplasia detection. *Biomed Res Int* 2014; 2014: 341483.
41. Rasoolimoghadam M, Safdari R, Ghazisaeidi M, Maharanitehrani M, Tahmasebiyan S. Designing decision support system to detect drug interactions type 2 diabetes. *Acta Inform Med* 2015; 23(6): 336-8.
  42. Walker JG, Licqurish S, Chiang PP, Pirota M, Emery JD. Cancer risk assessment tools in primary care: a systematic review of randomized controlled trials. *Ann Fam Med* 2015; 13(5): 480-9.
  43. Exarchos KP, Goletsis Y, Fotiadis DI. Multiparametric decision support system for the prediction of oral cancer reoccurrence. *IEEE Trans Inf Technol Biomed* 2012; 16(6): 1127-34.
  44. Kourou K, Exarchos TP, Exarchos KP, Karamouzis MV, Fotiadis DI. Machine learning applications in cancer prognosis and prediction. *Comput Struct Biotechnol J* 2015; 13: 8-17.
  45. Ayer T, Alagoz O, Chhatwal J, Shavlik JW, Kahn CE, Jr., Burnside ES. Breast cancer risk estimation with artificial neural networks revisited: Discrimination and calibration. *Cancer* 2010; 116(14): 3310-21.
  46. Park K, Ali A, Kim D, An Y, Kim M, Shin H. Robust predictive model for evaluating breast cancer survivability. *Eng Appl Artif Intell* 2013; 26(9): 2194-205.
  47. Holt TA, Thorogood M, Griffiths F, Munday S, Friede T, Stables D. Automated electronic reminders to facilitate primary cardiovascular disease prevention: Randomised controlled trial. *Br J Gen Pract* 2010; 60(573): e137-e143.
  48. Gilutz H, Novack L, Shvartzman P, Zelingher J, Bonne DY, Henkin Y, et al. Computerized community cholesterol control (4C): Meeting the challenge of secondary prevention. *Isr Med Assoc J* 2009; 11(1): 23-9.
  49. Hanahan D, Weinberg RA. The hallmarks of cancer. *Cell* 2000; 100(1): 57-70.
  50. Hanahan D, Weinberg RA. Hallmarks of cancer: The next generation. *Cell* 2011; 144(5): 646-74.
  51. Pasini FS, Maistro S, Snitcovsky I, Barbeta LP, Rotea Mangone FR, Lehn CN, et al. Four-gene expression model predictive of lymph node metastases in oral squamous cell carcinoma. *Acta Oncol* 2012; 51(1): 77-85.
  52. Fang L, Sun L, Hu FF, Chen QE. Effects of FasL expression in oral squamous cell cancer. *Asian Pac J Cancer Prev* 2013; 14(1): 281-5.
  53. Randhawa V, Acharya V. Integrated network analysis and logistic regression modeling identify stage-specific genes in Oral Squamous Cell Carcinoma. *BMC Med Genomics* 2015; 8: 39.
  54. Tang XH, Urvalek AM, Osei-Sarfo K, Zhang T, Scognamiglio T, Gudas LJ. Gene expression profiling signatures for the diagnosis and prevention of oral cavity carcinogenesis-genome-wide analysis using RNA-seq technology. *Oncotarget* 2015; 6(27): 24424-35.
  55. Jiang Q, Yu YC, Ding XJ, Luo Y, Ruan H. Bioinformatics analysis reveals significant genes and pathways to target for oral squamous cell carcinoma. *Asian Pac J Cancer Prev* 2014; 15(5): 2273-8.
  56. Liu Y, Liu CX, Wu ZT, Ge L, Zhou HM. Mining proteins associated with oral squamous cell carcinoma in complex networks. *Asian Pac J Cancer Prev* 2013; 14(8): 4621-5.
  57. Mehrotra R, Gupta DK. Exciting new advances in oral cancer diagnosis: Avenues to early detection. *Head Neck Oncol* 2011; 3: 33.
  58. Quaglini S, Sacchi L, Lanzola G, Viani N. Personalization and patient involvement in decision support systems: current trends. *Yearb Med Inform* 2015; 10(1): 106-18.
  59. Mertz E, Bolarinwa O, Wides C, Gregorich S, Simmons K, Vaderhobli R, et al. Provider attitudes toward the implementation of clinical decision support tools in dental practice. *J Evid Based Dent Pract* 2015; 15(4): 152-63.
  60. Meulendijk MC, Spruit MR, Willeboordse F, Numans ME, Brinkkemper S, Knol W, et al. Efficiency of clinical decision support systems improves with experience. *J Med Syst* 2016; 40(4): 76.
  61. Kesselheim AS, Cresswell K, Phansalkar S, Bates DW, Sheikh A. Clinical decision support systems could be modified to reduce 'alert fatigue' while still minimizing the risk of litigation. *Health Aff (Millwood)* 2011; 30(12): 2310-7.
  62. Mohammadzadeh N, Safdari R, Baraani A, Mohammadzadeh F. Intelligent data analysis: The best approach for chronic heart failure (CHF) follow up management. *Acta Inform Med* 2014; 22(4): 263-7.
  63. Safdari R, Kadivar M, Langarizadeh M, Nejad AF, Kermani F. Developing a Fuzzy Expert System to predict the risk of neonatal death. *Acta Inform Med* 2016; 24(1): 34-7.