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Chapter 1

HEAT-SHOCK PROTEIN 90 (HSP90) AND CANCER

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1. Introduction

Chaperones are highly conserved and play an important role to prevent the misfolding of proteins. The proteins can become misfolded due to the structural abnormalities in their function, location, or concentration (Macario & Conway de Macario, 2005). Thus, chaperones help to refold the misfolded proteins or they direct them to the ubiquitin proteolysis pathway for degradation (Rappa et al., 2013; Macario et al., 2013).

Heat shock proteins (HSPs) are a large family of molecular chaperones that are classified on their molecular weight that is expressed in kilodaltons (kDa). This family includes HSP10 (HSPE), HSP20 (HSPB), HSP40 (DNAJA, DNAJB, and DNAJC), HSP60 (HSPD), HSP70 (HSPA), HSP90 (HSPC), and small HSPs (Kampinga et al., 2009). A group of HSPs is known as small heat shock proteins (sHSPs) and is expressed in both prokaryotes and eukaryotes (Chatterjee and Burns, 2017). A member of the sHSP family, HSP27 (HSPB1) is known as a redox-sensitive molecular chaperone with a similar structure between the other sHSP members. HSP27s that often act to correct folding of proteins and induce proteolytic degradation of unstable or misfolded proteins by proteasome, are ATP-dependent chaperones (Kostenko and Moens, 2009). HSPs are highly conserved across all cellular organisms and have a role in various cellular processes including transporting proteins through membranes, protecting, and controlling their structure or presenting antigens (Singh et al., 2017).

HSPs are overexpressed in several tumors such as colon, lung, breast, and other cancers (Wu et al., 2017). Their elevated secretion by cancer cells facilitates targeting of these cells by natural killer cells. In addition, an increased levels of HSPs can promote cell proliferation, differentiation, and spreading, as well as resistance to apoptosis and poor prognosis (Hartl, 1996) so it is resulted with several neurodegenerative disorders such as motor neuron, frontotemporal lobar degeneration, Huntington's, Alzheimer's and Parkinson's diseases (Wu et al., 2017). HSPs inhibit proapoptotic molecules and maintain a balance between cell death and survival. Due to their roles in cancerous cells, HSPs are central targets in cancer therapeutics. Studies have shown that HSP27, HSP60, HSP70, and HSP90 differ depending on the type of cancer and are implicated in pathogenic mechanisms such as epithelial-mesenchymal transition (EMT), metastasis, and resistance to therapy (Calderwood et al., 2006; Lianos et al., 2015). Moreover, the increased and phosphorylated status of HSP27 is a predictor in many cancer tissues including epithelial ovarian cancer (Zhao et al., 2014), non-small cell lung cancer (NSCLC) (Sheng et al., 2017), thymic epithelial tumors (Janik et al., 2016), colon cancer (Bauer et al., 2012), cervical cancer (Jin et al., 2018), pancreatic ductal adenocarcinoma (PDAC), (Drexler et al., 2020) and esophageal adenocarcinoma (EAC)

(Söderström et al., 2019). It is evidence that HSPs possess a role in programmed cell death in various cancer cell lines. A schematic illustration of the functions HSPs is given in Figure 1.

Thus, this chapter focuses on the importance of HSP90s, their roles in cancer and known anticancer inhibitors.

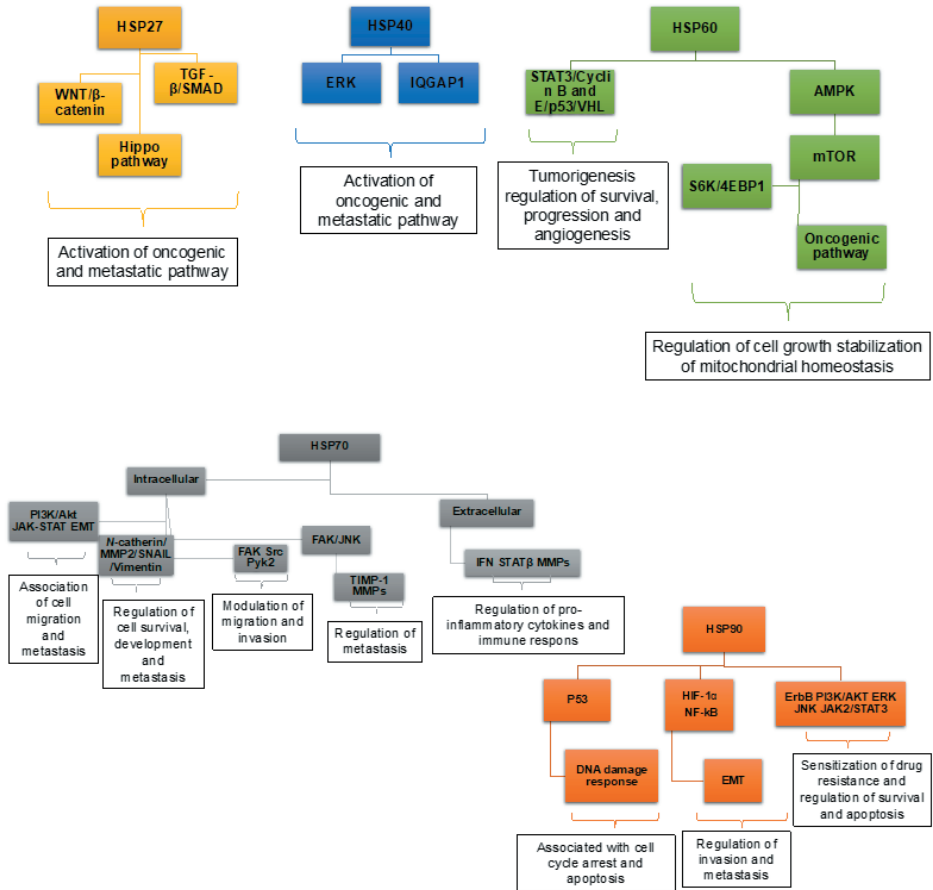


Figure 1. A schematic illustration of signaling pathways through HSPs (Adapted from Yun et al., 2020).

2. HSP90s as Heat Shock Proteins

The HSP90 family are involved in various cellular processes and are found in organisms from bacteria to humans. Normally, HSP90 contains approximately 2% of cellular proteins, but this can increase due to several factors such as hypoxia, inflammation, heavy metals, thermal stress, toxic agents, and cancer disease. In addition, HSP90 plays an important role in cellular homeostasis, cell survival, control of cell cycle, degradation of mutant proteins, hormone signalling, and apoptosis (Chiosis et al., 2006). HSP90 also contributes to adapt

for immunity by activating antigen presenting cells and dendritic cells. However, overexpression of HSP90 is associated with the development and progression of serious diseases including various types of cancer and neurodegenerative diseases. Many studies have reported that the targeting of HSP90 for related diseases is associated with their functions (Sumi and Ghosh, 2022).

HSP90 has ATP-independent chaperone activity and is distinguished from other HSPs such as HSP27 and HSP70. Furthermore, HSP90 can work together with HSP70 and other co-chaperones to reassociate misfolded proteins (Sims et al., 2011; Kanelaksis et al., 2000).

2.1. Structure of HSP90s

The HSP90 family contains different domains: the C-terminal domain (CTD), N-terminal domain (NTD), and middle domain (MD). The NTD binds to ATP. HSP90 inhibitors target the NTD competing with ATP for binding to the ATP-binding site. The CTD is responsible for dimerization and binding to client proteins and co-chaperones. The role of MD is ATP hydrolysis and substrate binding. HSP90 also has a small dynamic domain that connects the NTD to the MD (Birbo et al., 2021).

2.2. The Role of HSP90 Isoforms in Biological Processes

The function of HSP90 isoforms in biological processes has been extensively studied due to their canonical functions in maintaining protein homeostasis. The HSP90 family comprises five subfamilies that are located in different parts of cells including HSP90 α , HSP90 β , HSP90N isoforms, GRP94 (glucose-regulated protein 94) (HSP90B1), and TRAP1 (tumor necrosis factor receptor-associated protein 1). TRAP1 has a significant function in maintaining mitochondrial integrity and preventing mitochondrial apoptosis (Ramkumar et al., 2020; Matassa et al., 2018). HSP90 isoforms, functions and expression status are given in Table 1.

Table 1. *HSP90 isoforms, functions, and expression status (Eltaib et al., 2016)*

Isoforms	Expression status	Specific Functions
HSP90 α	Induced	<ul style="list-style-type: none"> • Cell growth • Regulation of cell cycle • Induction of stress • Cytoprotection
HSP90 β	Constitutive	<ul style="list-style-type: none"> • Early embryonic development • Germ cell maturation • Cytoskeletal stabilization • Cellular transformation • Long term cell adaptation
HSP90N	Constitutive	<ul style="list-style-type: none"> • Cellular transformation
TRAP1	Constitutive	<ul style="list-style-type: none"> • Regulation of cell cycle

2.3. HSP90s and Co-chaperons

HSP90 α and HSP90 β are mainly located in the cytoplasm and they play crucial roles in cellular processes such as signalling pathways, energy metabolism, and cell viability. During stressful conditions, HSP90 α is highly expressed and contains heat-inducible cis-acting elements whereas HSP90 β is constitutively expressed. The heat shock response (HSR) induces the expression of these proteins. HSP90 α (eHSP90 α) that is secreted in the extracellular region, have a role in the invasion of several types of cancer *in vitro* and *in vivo*. Hence, the blocking of eHSP90 α has been considered a rational way in cancer management. HSP90 α is also involved in restructuring client proteins into functional conformations (Saini et al., 2018).

The increased level of HSP90 α plays a significant role in metastasis and invasion of tumor cells. For instance, the activation of MMP-2 (matrix metalloproteinase-2) by HSP90 α is related to enhance the invasion of tumor cells. MMP-2 is responsible for digesting extracellular matrix components and cancer cells. HSP90 α also activates other extracellular proteins including plasminogen and tissue plasminogen activator protein (tPA) that play crucial roles during a lot steps of cancer metastasis and invasion (Neckers, 2007). These findings provide new insights into the potential of targeting HSP90 isoforms as a therapeutic strategy for cancer treatment.

3. The Role of HSP90 in Cancer

The role of HSP90 in cancer cells is essential due to their rapid proliferation rate, reduced control in protein synthesis quality, and increased cellular stress. HSPs are highly regulated and they are crucial for cellular survival under stressful conditions, and are implicated in the pathogenesis of most cancer types. HSPs take a part in various processes including cell proliferation, invasion, induction of angiogenesis, metastasis, and immune tolerance (Lin et al., 2020; Xu et al., 2017).

HSP90 is one of the key factors in cellular survival under stressful conditions, regulates the expression of more than 200 proteins known as “HSP90 client proteins”. These client proteins participate in signalling and other vital pathways (Li and Buchner, 2013). It was indicated that the expression of HSP90 was higher in cancer cells, and increased levels of HSP90 were found in numerous tumor cells including various types of cancer. High level of HSP90 is associated with a poor prognosis. It is indicated that the high expression of HSP90 is associated with a less favourable response to anti-neoplastic treatment, and it exists as a multichaperone complex (Trepel et al., 2010).

Additionally, miRNAs have been found with their function as tumor suppressors by targeting HSP90's 3'-UTR. For instance, miR-223 negatively correlates with HSP90B1 expression and promotes apoptosis through the

PI3K/Akt/mTOR signalling pathway while inhibiting cell growth. Similarly, miR-628-3-p promotes apoptosis and inhibits the migration of A549 cells. On the other hand, miR-29a suppresses several members of the HSP family including HSP27, HSP40, HSP70, and HSP90. Increased level of HSP90 cause via PI3K/Akt/mTOR signalling pathway inducing autophagy-inducing chemoresistance in osteosarcoma (Xiao et al., 2018).

p23 is an essential component of the HSP90 chaperon complex, is one of HSP90's co-chaperones. It has upregulated expression in cancer cells including metastatic lung cancer, breast cancer, and prostate carcinoma, promotes cell adhesion, invasion, and lymph node metastasis. A study on childhood acute lymphoblastic leukemia (ALL) has indicated that the regulation of p23 has carried out by miR-101. The experimental results have shown that miR-101 negatively regulates p23. On the other hand, it is indicated that various miRNAs have a significant impact on the regulation of HSPs or their co-chaperones (Pan et al., 2018; Okusha et al., 2022; Holt et al., 1999). A schematic representation of miRNA targeting HSPs in cancer treatment is shown in Figure 2.

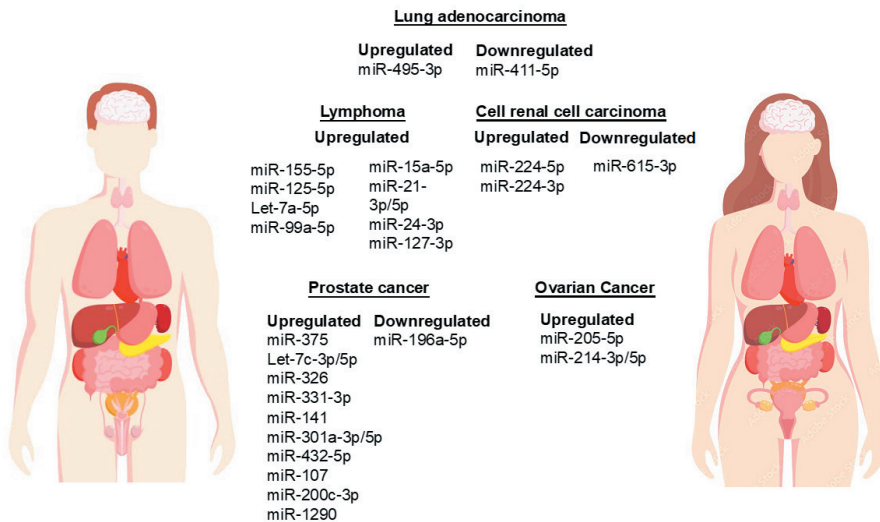


Figure 2. miRNA targeting HSPs in cancer (adapted from Albakova et al., 2021).

The T53 gene and p53 are client proteins of HSP90 and their relationship has been linked to cancer development. In the increased stress conditions, the function of p53 is highly dependent on Hsp90. When the capacity of Hsp90 is overwhelmed and the TP53 gene is mutated, it can result with the rapid dysregulation and degradation of p53, leading to the loss of tumor suppress functions. Additionally, cancer-inducing mutations in TP53 increase the binding affinities of Hsp90 and p53 (Hagn et. al., 2010) It was indicated that HSP90 play an important role on stabilizing and interacting with PKM2 in hepatocellular carcinoma cells that is associated with the activity of GSK-3β

and the phosphorylation of PKM2 at Thr328. The survival of leukemia cells is promoted by HSP90 via binding to APAF-1 and BCL-2 (Dias et al., 2002).

Steroid hormone receptors such as glucocorticoid receptor (GR), androgen receptors, progesterone receptors, mineralocorticoid receptors, and estrogen receptors form a complex with HSP90 for protecting its role. The specific HSP90 inhibitors can affect the structure and function of related receptors (Zabinsky et al., 2019; Kaziales et al. 2020). HSP90 is also associated with epigenetic regulators such as UHRF1 and BRCA2, and transcriptional factors and the activation of cytokine signalling. Moreover, HSP90 can cooperate with calcineurin and Tau proteins in pathological conditions. It is resulted with the promising target for cancer and neurodegenerative diseases (Miyata et al., 2012, 2011).

Macrophage migration inhibitory factor (MIF) plays an important role in regulating innate immunity. However, its expression is known to increase in certain types of cancer including breast cancer due to its interaction with HSP90-associated chaperones. Recent studies conducted on human colorectal cancer (CRC) cells have suggested that MIF promotes angiogenesis, proliferation, and migration by binding to its main receptor CD74. This binding triggers the activation of p38, MAPKs, or PI3K/AKT, leading to the expression of angiogenic factors. In addition, MIF has been found to regulate therapeutic resistance through its effects on STAT3, MAPKs, AMPK, or hypoxia-dependent mechanisms (Biebl and Buchner, 2019; Trepel et al., 2010). A schematic illustration for signalling pathways is given in Figure 3.

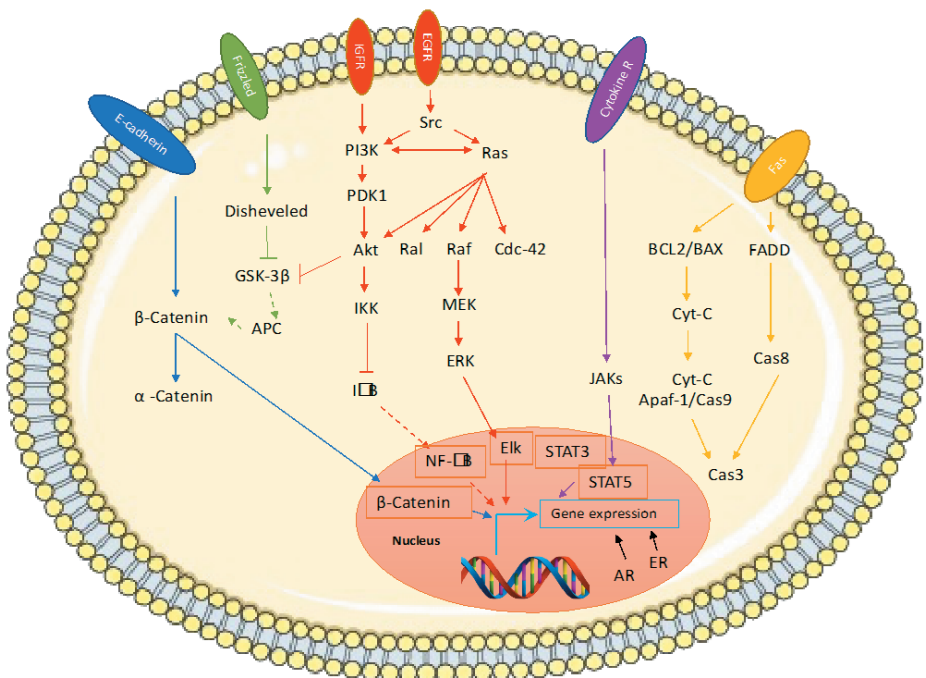


Figure 3. HSP-related signalling pathways (adapted from Hoter & Naim, 2019)

3.1. HSP90 Inhibitors

HSP90 inhibitors are developed to prevent tumor-prompting signalling pathways and interrupt the function of HSP90 in tumor cells. Up to date, several HSP90 inhibitors have been developed and reported to be used in the treatment of cancer (Birbo et al., 2021; Fuhrmann-Stroissnigg et al., 2017; Kim et al., 2009; Yang et al., 2022). Table 3 shows HSP90 inhibition for cancer therapy (Yun et al., 2020). Therefore, HSP90 has been identified as a significant drug target. The first inhibitor of HSP90 is geldanamycin (GA) that is a naturally occurring compound having benzoquinone ring. GA binds to ATP binding site of *N*-domain of HSP90 (Hadden et al., 2006). Due to the restrictions such as hepatotoxicity and low solubility of GA, it is determined as an inadequate candidate for clinical applications (Supko et al., 1999). Then, its derivatives were synthesized to be used in preclinical and clinical studies (Niikura et al., 2006). Another natural compound is Radicicol isolated from fungus was displayed potent *in vitro* antiproliferative activity. Because of its low biological stability, its derivatives were synthesized to test *in vivo* efficacy (Birbo et al., 2021). Radanamycinamide showed potent inhibitor activity at low concentrations in breast cancer cell lines. The inhibitor, PU3 that binds to *N*-terminal domain of HSP90, has been reported with its ability to inhibition of the growth of breast cancer cells (Chiosis et al., 2001). One of natural compound is novobiocin that has a coumarin scaffold targets HSP90 CTD (Marcu et al., 2000). Similarly, clorobiocin and coumermycin A1 are coumarin antibiotics and show increasing activity compare to novobiocin (Marcu et al., 2000). One of HSP90 inhibitor, gamitrinib targets mitochondrial HSP90 and is known as a selective inhibitor (Birbo et al., 2021; Fiesel et al., 2017). Structures of above mentioned some HSP90 inhibitors are given in Figure 4.

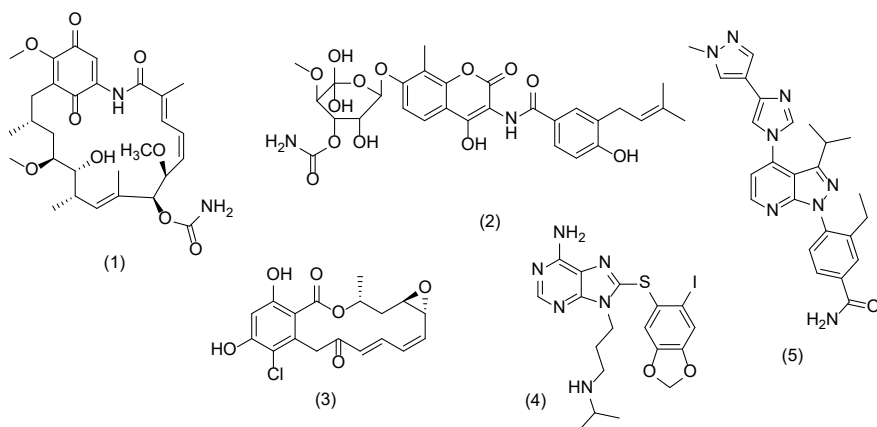


Figure 4. Structures of some known HSP90 inhibitors. (1) Geldanamycin, (2) Novobiocin, (3) Radicicol, (4) PU-H71, (5) TAS-116.

Table 3. *HSP90 inhibition for cancer therapy (Yun et al., 2020)*

Cancer Type	Inhibitor	Result	Reference
Thyroid, breast lung and ovarian cancer	Ganetespib	<ul style="list-style-type: none"> ↓ cell proliferation, metastasis, tumor growth • induction of cell cycle arrest 	Lin et al., 2017; Ray-Coquard et al., 2019; Mumin et al., 2019
Papillary thyroid carcinoma	NVP-AUY922	<ul style="list-style-type: none"> ↓ cell viability • apoptosis induction, • suppress survivin 	Liu et al., 2017
Gastric cancer an NSCLC	NVP-AUY922	<ul style="list-style-type: none"> ↓ tumor growth angiogenesis, metastasis 	Lee et al., 2011; Jensen et al., 2008
Small cell lung cancer	NVP-AUY922 and BCL-2 inhibitor ABT-737	<ul style="list-style-type: none"> • induction of apoptosis, ↓ ABT-737 drug resistance, downregulation of AKT and ERK 	Yang et al., 2017
Chronic lymphocytic leukemia	PU-H71	<ul style="list-style-type: none"> ↓ B-cell receptor kinase, PI3K/mTOR pathway • induction of apoptosis 	Guo et al., 2017
Ovarian cancer	Geldanamycin	<ul style="list-style-type: none"> ↓ paclitaxel sensitivity tumor growth • inactivation of p38/H2AX 	Mo et al., 2016; Supko et al., 1995
Pancreatic cancer	Gambogic acid (selective HSP90β inhibitor)	<ul style="list-style-type: none"> ↓ cell growth • induction of cell cycle arrest and apoptosis • regulate ERK/E2F1/RRM2 signaling pathway 	Makhlough et al., 2017
Prostate cancer	KU675	anti-proliferative and cytotoxic activity	Camilleri et al., 2016
Prostate cancer	SM253 and SM258	<ul style="list-style-type: none"> • Suppress cell proliferation • induction of apoptosis 	Arnold et al., 2017
Triple-negative breast cancer	L80	<ul style="list-style-type: none"> ↓ cell proliferation • regulate AKT/MEK/ERK/JAK2/STAT3 signaling pathway 	Cho et al., 2019
Lung and gastric cancer	TAS-116 (selective HSP90α and β inhibitor)	anticancer activity	Holohan et al., 2013; Vyas et al., 2016
Breast and prostate cancer	GRP94 (selective inhibitor)-polyclonal antibody	anticancer activity	Guaragnella et al., 2014

CONCLUSION

Cancer is a major public problem in worldwide. The number of deaths from cancers is increasing day by day. For instance, according to United States analysis for various cancer types, it is estimated that 1,958,310 new cancer cases and 609,820 cancer deaths can be occurred in this year (Siegel et al., 2023). There is needed new targets and strategies to be used for the treatment of cancer. The importance of HSP90 in cancer researchers have increased. In addition, patient-derived studies showed that HSPs had potential role for early detection of cancer. Therefore, HSP90 has become a significant drug target in the role of cancer progression, metastasis, and invasion. This chapter mentions that the biological functions, structure, the association with co-chaperons and significance in cancer of HSP90 and its inhibitors for targeted cancer therapy. The studies show that HSP90 is a promising target for cancer therapy.

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Chapter 2

CURRENT APPROACHES TO EARLY CHILDHOOD CARIES MANAGEMENT

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Introduction

Dental caries is a common and preventable disease in which biological, behavioral and environmental factors are effective. This disease causes health problems such as pain and infection in children and reduces their quality of life. In addition to physiological problems, it also creates various social and psychological problems in children. For these reasons, it is necessary to prevent dental caries and to treat existing caries with appropriate treatment approaches so that children can grow and develop in a healthy way, both physically and psychologically. After determining the biological risk factors, environmental risk factors and protective factors of the child, dental caries can be prevented with personalized treatment methods. In order to determine these factors, a risk assessment should be made using a caries risk assessment tool. Many caries risk assessment forms have been developed for this purpose. The “CAMBRA” method, one of them, is a current approach option for caries risk assessment. In the “CAMBRA” method, personalized caries management approaches are applied according to the caries risk level of the individual, after the caries risk assessment. A three-stage (primary, secondary and tertiary prevention) path is followed in the fight against early childhood caries, which is a very common type of caries in children all over the world. Primary prevention includes awareness of breastfeeding, dietary habits, oral health, and oral hygiene practices. Secondary protection includes applications consisting mainly of fluoride varnishes, pit and fissure sealant applications. Tertiary prevention aims to treat cavitated caries lesions with silver diamine fluorides (SDF) applications, atraumatic restorative treatment (ART), minimally invasive restorations, and pediatric crowns.

1. Dental Caries

The development of carious lesions in dental tissues involves a dynamic process in which acids resulting from bacterial fermentation of dietary carbohydrates affect the demineralization of inorganic parts of dental tissues (Bradshaw and Marsh, 1998). As acid attacks continue, microorganisms with high acid tolerance emerge, disrupting the pH balance, causing demineralization to dominate in the demineralization-rem mineralization cycle. This causes the loss of the mineral content of the tooth as the physiological balance between the mineral structure of the tooth and the oral microbial biofilm is disrupted (Van Ruyven et al., 2000).

Microorganisms in dental plaque on tooth surfaces can produce organic acids, which are by-products such as lactic acid, propionic acid, acetic acid, as a result of carbohydrate fermentation (Yağın Çakır et al., 2010). These organic acids cause the pH value, which is 7.0 under normal conditions, to fall below the critical pH value of 5.5 (Caufield et al., 2005).

When the pH value decreases, the demineralization process begins in the dental tissues with the dissolution of calcium and phosphate ions from the hydroxyapatite crystals, which constitute the majority of the inorganic part of the tooth enamel (Garcia-Godoy and Hicks, 2008). However, when there are conditions that will increase the decreasing pH value, the dissolved mineral can precipitate on the tooth surface again, and this creates the remineralization process (Matsui and Cvitkovitch, 2010). The mechanism of dental caries develops depending on the balance between demineralization and remineralization processes (Touger-Decker and Van Loveren, 2003).

1.1. Etiology of dental caries

Dental caries is a multifactorial disease caused by many factors. Caries formation requires host (tooth), caries-causing microflora (such as *Streptococcus mutans*, *Lactobacilli*), fermentable carbohydrates and time (Harris et al., 2004). Apart from these, factors that accelerate or slow down the formation of dental plaque, such as saliva, tooth morphology, oral hygiene, nutritional habits, immune system, education level, lifestyle, socioeconomic status and fluoride use (F) are secondary factors that indirectly affect the caries formation mechanism (Figure 1) (Richards et al., 2017).

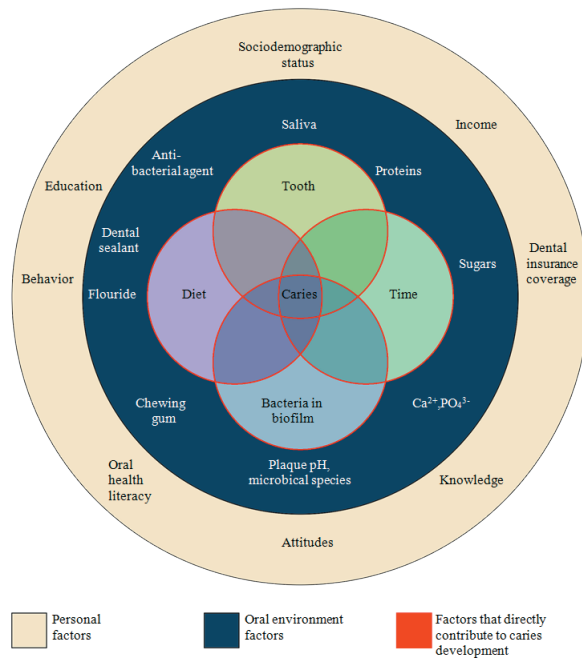


Figure 1: Common factors causing dental caries

1.2. Dental plaque and biofilm

Dental plaque is one of the factors that play a role in the onset of dental caries, as it reduces the washing and buffering effect of saliva, as well as because it contains acidogenic microorganisms and allows dental tissues to interact with the acid that occurs for a long time (Wang et al., 2018). In addition, dental caries is defined as a biofilm-induced infectious disease of the oral cavity (Pitts et al., 2017).

- The salivary proteins and glycoproteins precipitated by selective adsorption on dental tissues form pellicle, an organic accumulation. This membrane has a thickness of 0.1-1.0 millimeters (mm) and is insoluble in oral fluids. It is formed rapidly by the precipitation of mucin proteins found in the saliva structure on the cleaned tooth surfaces (Hicks et al., 2003). It contains IgA, amylase, lysozyme, histatin, cystatin, statherin, bacteria-derived glucosyl transferases and proline-rich proteins. Pellicle has many biological benefits through various mechanisms in protecting the enamel surface and providing remineralization. However, in addition to these positive properties, pellicle is effective in the adhesion of microorganisms in the mouth to tooth surfaces with electrostatic, hydrophobic ion and van der Waals forces. With the attachment of bacteria to this pellicle layer and the precipitation of other bacteria and proteins in saliva, plaque thickness and mass increase. The first component of the plaque is the physiologically formed mucin layer. The second formed after this is the pathological microbial component formed by the precipitation of bacteria (Lenander-Lumikari and Loimaranta, 2000). This situation reveals that the plaque has two components. As a result of the adhesion of new bacteria to the microbial component, the diversity in the plaque microflora increases, and a stable biofilm layer begins to form with the realization of late bacterial colonization (Garcia-Godoy and Hicks, 2008). Acid production by bacteria in the biofilm during carbohydrate metabolism is one of the main virulence factors in which lactate dehydrogenase (LDH) plays a critical role (Beloin and Ghigo, 2005). Another virulence factor is the capacity of these bacteria to produce glucosyl transferase (GTF) (Paes Leme et al., 2006). Bacteria catalyze the synthesis of intracellular polysaccharide (IPS) and extracellular polysaccharide (EPS) from sucrose through this enzyme (Bowen and Koo, 2011). Extracellular polysaccharides (EPS), especially water-insoluble glucans, contribute significantly to biofilm formation and its structural integrity. In addition, thanks to glucans, adhesion of bacteria to the tooth surface and adhesion between bacteria are provided (Ahn et al., 2018). For this reason, removal of dental plaque from tooth surfaces in order to suppress cariogenic virulence factors of bacteria in biofilm is seen as the most effective approach in the importance of dental caries (Garcia-Godoy and Hicks, 2008; Bowen and Koo, 2011).

2. Early Childhood Caries (ECC)

Early childhood caries (ECC) is a severe and specific form of dental caries that has a multifactorial nature and affects the primary teeth of infants and preschoolers (Zaror et al., 2022). ECC is defined as “the presence of one or more decayed (non-cavitated or cavitated lesions), missing (due to caries) or filled tooth surface in any primary tooth in a child under six years of age” (Marino et al., 2023).

The following 3 different definitions can be made for severe ECC:

- 1) Any smooth surface caries in children younger than 3 years old
- 2) Presence of 1 or more caries, missing or filled in primary maxillary anterior teeth in children aged 3-5 years
- 3) The number of caries, extracted or filled teeth due to caries is at least 4 in children of 3 years of age, at least 5 in children of 4 years of age, and at least 6 in children of 5 years of age (AAPD, 2021a).

ECC is characterized by early onset and rapid progression in young children, and eventually causing complete destruction of primary teeth (Shmoeckel et al., 2020; Machiulskiene et al., 2020). It is a dangerous form of caries. It begins immediately after dental eruption, develops on smooth surfaces, progresses rapidly and leaves a lasting effect on the dentition. Caries that affect primary teeth in infants and toddlers also cause permanent teeth to decay. ECC does not only affect the teeth, it affects the whole health in terms of its consequences (Zaror et., 2022; Schmoeckel et al., 2020).

2.1. Etiology

ECC etiology is complex and includes socioeconomic, biological and behavioral factors (Kirthiga et al., 2019) (Figure 2). Factors such as presence of hypoplasia, presence of visible dental plaque, low socioeconomic status, frequent exposure to sugary snacks and beverages between meals, and prolonged breastfeeding (more than 12 months) are strongly associated with ECC (Tinanoff et al., 2019).

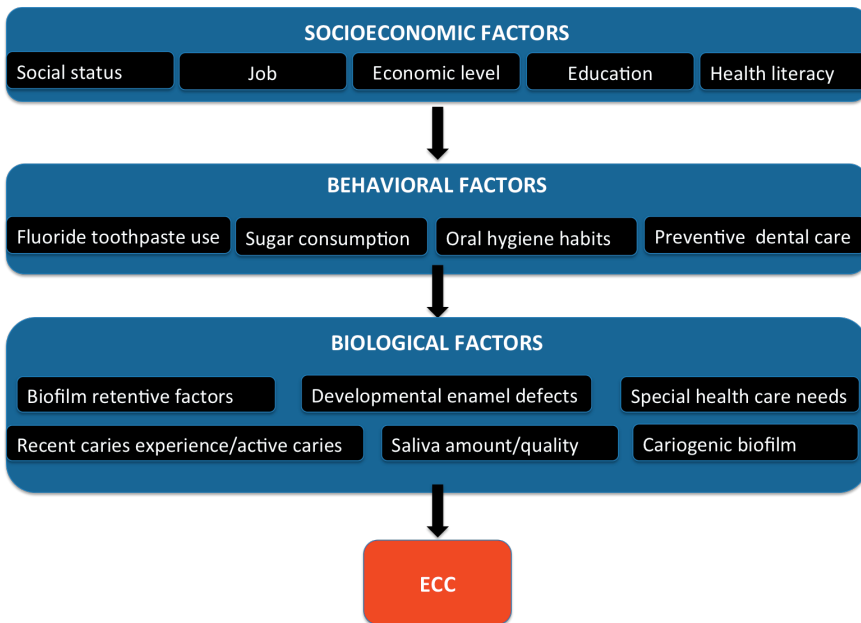


Figure 2: Socioeconomic, behavioral and biological factors associated with ECC

Demineralization of enamel is caused by acid-producing bacteria that ferment dietary carbohydrates. After ingestion of carbohydrates, particularly sucrose, the pH in tooth-adherent biofilms drops rapidly to 5.0 or below. Low pH leads to the dysbiotic microbiome, which is characterized by increased proportion of acidic biofilm species and changes in the composition of the biofilm matrix. Therefore, frequent exposure to sugar leads to continuous acid production and demineralization of the tooth (Tinanoff et al., 2019).

Consumption of free sugars (i.e. sugars added to foods and beverages, naturally occurring sugars in fruits, honey, syrups, juices), age at which sugar is used, and frequency of consumption are critical to the development of dental caries. In relation to the transition to sugar in the first years of life, dietary patterns characterized by a large number of highly sweetened foods and beverages have been associated with the incidence of childhood caries in later years. In addition, bottle feeding and breastfeeding after 12 months, especially frequent and nighttime breastfeeding, are associated with ECC (Moynihan et al., 2014, Chaffee et al., 2015b; Feldens et al., 2018; Peres et al., 2018). The influence of intraoral factors, such as developmental defects of enamel, is also considered a risk factor for ECC. Loss of surface

integrity and mineralization deficiencies in enamel explain the high risk of ECC in children affected by developmental defects (Seow et al., 2016). Socioeconomic factors such as maternal education and ethnicity are associated with the prevalence of ECC.. Because these factors affect parents' attitudes and practices, including diet and hygiene practices that they undertake with their children, as well as parents' knowledge (Kramer et al., 2015).

3. Caries Risk Assessment (CRA)

Caries risk assessment (CRA) is defined as the process of determining the probability of a patient developing new carious lesions and/or a change in the severity and/or activity of existing lesions within a given period of time (Fontana et al., 2006). The CRA recommends individualized preventive and therapeutic strategies to reduce the specific factors thought to be associated with dental caries in different risk categories and to reduce the level of caries risk. Individual risk assessment constitutes the cornerstone of the treatment plan for the management of early childhood caries for pediatric patients (Twetman, 2016). According to the risk assessment system, caries management aims to protect healthy teeth and contribute to the prevention of dental caries.

Dental caries develops depending on the balance between pathological and protective factors shown in Figure 3 (Featherstone, 2003). Therefore, during the dental examination, the clinician should consider risk and protective factors together to assess the child's caries risk (Tinanoff et al., 2019).

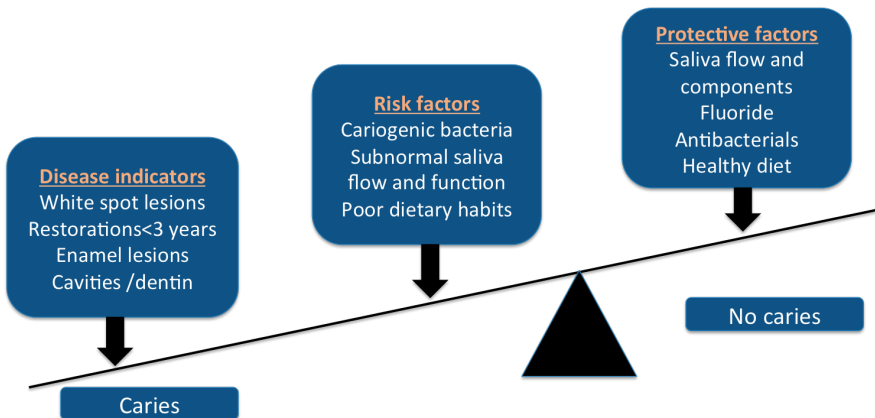


Figure 3: *The caries imbalance*

Therefore, during the dental examination, the clinician should consider risk and protective factors together in order to evaluate the child's caries

risk (Tinanoff et al., 2019). Among the risk factors, non-cavitated lesions, visible carious cavities, enamel defects, filled or extracted teeth, and the presence of plaque on the visible tooth surface should be examined in clinical examination. As protective factors, the child's drinking water with fluoride, brushing teeth twice a day with fluoride toothpaste, professional topical fluoride applications, and regular dental care behaviors should be questioned (Featherstone, 2003). Apart from these, economic status of the family or caregiver, low health literacy, frequent exposure of the child to foods and beverages containing sugar, feeding frequently or before bedtime with sugar-containing formula, frequent and night breastfeeding after 12 months, the presence of active dental caries in the mother or primary caregiver and the child's special health problems are among the factors that should be examined in caries risk assessment (Moynihan et al., 2004; Feldens et al., 2018).

Caries risk assessment should ideally be comprehensively performed during the first dentist visit prior to illness. Since the risk category will change over time, the risk of caries should be evaluated in the first year of life and then repeated periodically (Fontana et al., 2006).

3.1. Caries risk models and tools

A wide variety of CRA models have been created around the world regarding the ECC, including the caries management by risk assessment (CAMBRA), caries risk assessment tool (CAT), American Dental Association (ADA) caries risk assessment, National University of Singapore (NUS) model, Dundee Caries Risk assessment model (DCRAM), and Cariogram (Zero et al., 2001; Nicolau et al., 2003; Featherstone, 2004; AAPD, 2014).

3.2. CAMBRA

CAMBRA is an evidence-based risk assessment tool for the prevention and treatment of caries in the earliest stages, rather than waiting for irreversible damage to the teeth (Featherstone et al., 2004). CAMBRA was published in 2007 in the Journal of the California Dental Association. It has also been updated for the patient age group from 6 years to adults in 2019, and a risk assessment form is provided for both age ranges, 0-6 years and 6 years to adulthood (Fearherstone et al., 2019a; Jenson et al., 2007). This risk assessment tool is used in various dental faculties and community health centers around the world for young children aged 0-6 (Ramos-Gomez et al., 2007; Featherstone and Chaffee, 2018; Ramos-Gomez et al., 2017; Ramos-Gomez et al., 2014). The CAMBRA risk assessment form for children aged 0-6 is shown in Table 1 (Featherstone et al., 2019b).

Table 1. Updated “CAMBRA” caries risk assessment form for ages 0-6 years

Patient Name:	Reference Number:		
Provider Name:	Date:		
Caries risk assessment component* (Check yes only in appropriate shaded column)	Column 1	Column 2	Column 3
	Score: -1	Score: +2	Score: +3
Biological or environmental risk factors** Question Items		Check if Yes*	
1. Frequent snacking (more than 3 times daily)			
2. Uses bottle/non-spill cup containing other than water			
3. Parent/primary caregiver or sibling has current decay or a recent history of decay (see high risk description below)			
4. Family has low socioeconomic &/or low health literacy status			
5. Medications that induce hyposalivation			
Protective factors - Question Items	Check if Yes*		
1. Lives in a fluoridated drinking water area			
2. Drinks fluoridated water			
3. Uses fluoride (F)-containing toothpaste at least two times daily-a smear for ages 0-2 years and pea size for ages 3-6 years of 1,000 ppm F.			
4. Has had fluoride varnish applied in the last 6 months			
Biological risk factors - Clinical exam**		Check if Yes*	
1. Heavy plaque on the teeth			
Disease indicators - Clinical exam			Check if Yes*
1. Evident tooth decay or white spots			
2. Recent restorations in last 2 years (new patient) or the last year (patient of record)			
Column total score (Columns 2 + 3 -1):	Column 1 Total:	Column 2 Total:	Column 3 Total:
Yes's in columns 1 and 2 only; use the caries balance-below Yes or yes's in column 3 likely indicates high or very high risk			

Final Overall Caries Risk Assessment Category (check) determined as per guidelines below

LOW MODERATE HIGH VERY HIGH

*Check only the yes answers in the appropriate shaded column. Enter the score of -1, +2 or +3 for each yes checked. Unshaded columns are left blank. Assess the caries risk as per instructions in Table 1 (part 2) below.

**Biological and environmental risk factors are split into (a) question items, (b) clinical exam.

‡Modified from Featherstone et al. [3] with permission of California Dental Association Journal.

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Refer to the second page of this form (part 2) for instructions for use as guidelines for caries risk assessment.

It is frequently used and recommended to evaluate caries risk in individuals from the age of six to adulthood (Featherstone et al., 2021). Successful management of dental caries depends on the use of a reliable CRA tool that allows for the determination of caries risk level and the preparation of a personalized treatment plan derived from the information learned during the CRA process (Featherstone et al., 2021). Each individual is evaluated using CAMBRA according to disease indicators, risk factors, and protective factors to calculate current and future caries risk, and the overall CAMBRA method includes both risk assessment and caries management (Chaffee et al., 2015a).

Table 2. Caries risk assessment guidelines 0-6 years

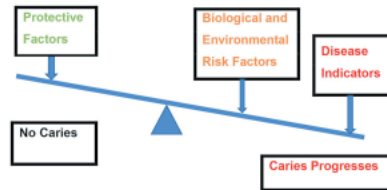
The dental caregiver has the responsibility of making a caries risk assessment and then deciding on a caries management plan for the patient that leads from the risk assessment and a personalized assessment of the needs of the individual patient. These guidelines can assist in the process.

Determining the caries risk as low, moderate, high or very high - guiding principles.

1. Low risk. If there are protective factors, very low or no risk factors, no disease indicators, and the protective factors prevail, the patient is at low risk.
2. Moderate risk. If there are no disease indicators and the risk factors and protective factors appear to be balanced then a moderate caries risk determination is appropriate. If in doubt move the moderate to a high classification.
3. High risk. If there is a "YES" in column 3 (one or both disease indicators) the patient is very likely at high risk. Even if there are no "yes" disease indicators the patient can still be at high risk if the risk factors definitively outweigh the protective factors. Parent or caregiver with current or recent dental decay most likely indicates high caries risk for the child.
4. Very high risk. If the above process indicates high risk and the existing or recent decay is severe and/or extensive a designation of "very high" caries risk is appropriate and will guide a more aggressive caries management plan.

Any items checked "yes" should also be used as topics to modify behavior or determine additional therapy.

Use the following modified caries balance to visualize the overall result and determine the risk level. It may be helpful to allocate scores for each "yes" checked on the risk assessment form with a score of -1 for yes's in column 1, and +2 and +3 respectively for yes's in columns 2 and 3. The final total will help guide the risk level decision. **Low** = -4 to -1; **Moderate** = 0 to +3; **High** = +4 to +13; **Very high** = +14 to +18 and/or is a high risk level plus extensive and/or severe recent or existing decay.



Additional caries-related components for caries management and caregiver/patient counseling.
Record in patient chart at each visit.

Dietary counseling to reduce frequency and amount of fermentable carbohydrates, especially sucrose, fructose (high fructose corn syrup) and continual fruit juice (e.g., apple juice). Record number and type of daily snacks, drinks and juices used.

Bottle used continually, bottle used in bed or nursing on demand. Record details provided.

Fluoride (F) toothpaste use. Note frequency and amount used at each visit.

Record all recommended therapy such as F toothpaste, F varnish, use of silver diamine fluoride in appropriate cases. Record usage provided by parent/caregiver.

Record medications at each visit and check for changes.

Record participation in assistance programs such as "school lunches," "head start," appropriate to the state or country.

Child has developmental problems/child has special care needs (CHSCN).

Inadequate saliva flow and related medications, medical conditions, or illnesses.

Discuss self-management goals with caregiver/patient and set two goals together at each visit. Provide in writing.

3.3. Caries risk assessment for the age group 0–6 years

Caries risk assessment is the first of the 6 steps of the oral care visit for 0-6 year olds. These 6 steps are listed as follows:

1. Initiation of caries risk assessment
2. Knee-to-knee position for oral examination
3. Toothbrush prophylaxis
4. Clinical examination
5. Determination of caries risk level
6. Self-management goals (predictive guidance) (Featherstone et al., 2019a).

In the CRA procedure created for the 0-6 age group shown in Table 2 (Featherstone et al., 2021), the caries risk groups for this age group are defined as low, medium, high and very high. Determination of caries risk level is guided by the visualization of caries balance based on clinical observations and results in the caries risk assessment form, in addition to written guidelines (Featherstone et al., 2021).

3.4. Caries management in children after risk assessment

Evaluation of caries risk levels for the formation of new carious lesions is an important stage in the management of dental caries and in improving oral health. It is recommended to perform the first oral examinations after the eruption of the first tooth or within the first 1 year of life in order to provide caries management by giving priority to preventive treatments before the need for dental treatment arises (Ramos-Gomes and NG, 2011). Successful management of dental caries requires a risk-based approach to devise a treatment plan that targets the biological and environmental factors contributing to the disease (Featherstone et al., 2021). In other words, determining the level of caries risk enables the creation of a personalized caries management approach for patients (Featherstone et al., 2021). Table 3 shows caries treatment management according to risk groups.

Table 3. Caries management according to risk groups

Risk Group	Age	Diagnostics		Preventive Interventions			Operative Interventions
		Periodic oral examination	Radiographs	Fluoride	Diet	Sealant	
<i>Low</i>	1-2 year olds	6-12 months	-	Brush twice a day with fluoridated toothpaste	Counseling	-	Surveillance: periodic monitoring
	3-5 year olds	6-12 months	-	Brush twice a day with fluoridated toothpaste	Counseling	-	Surveillance: periodic monitoring
<i>Moderate</i>	1-2 year olds	6 months	-	Brush twice a day with fluoridated toothpaste Fluoride supplements Fluoride varnish every 6 months	Counseling	-	Active surveillance: regular monitoring
	3-5 year olds	6 months	6-12 months	Brush twice a day with fluoridated toothpaste Fluoride supplements Fluoride varnish every 6 months	Counseling	On enamel defects, at risk pits and fissures	Active surveillance: regular monitoring, restore cavitated enlarging lesions

High	1-2 year olds	3 months	-	Brush twice a day with fluoridated toothpaste Fluoride varnish every 3 months	Counseling	-	Active surveillance Restore cavitated lesions (ATR, ITR, SDF)
	3-5 year olds	3 months	6 months	Brush twice a day with fluoridated toothpaste Fluoride supplements Fluoride varnish every 3 months	Counseling	On enamel defects, at risk pits and fissures	Active surveillance Restore cavitated lesions (ATR, ITR, SDF)
Very high	1-2 year olds	Monthly	-	Brush twice Daily with F toothpaste Fluoride supplements Fluoride varnish every 1-3 months	Counseling	-	Active surveillance Restore cavitated lesions (ATR, ITR, SDF)
	3-5 year olds	Monthly	6 months	Brush twice a day with fluoridated toothpaste Fluoride supplements Fluoride varnish every 1-3 months	Counseling	All pits and fissures	Active surveillance Restore cavitated lesions (ATR, ITR, SDF)

ATR, atravmatic restorative treatment; ITR, interim therapeutic restoration; SDF, silver diamine fluoride

4. Clinical Management of Early Childhood caries

4.1. Primary prevention

The key to reducing the prevalence of disease in ECC clinical management is primary prevention and should be initiated before disease onset. Health professionals in primary care should train parents and caregivers about oral and dental care. Awareness of caries risk factors and protective factors should be created (Albino et al., 2016).

4.1.1. Oral health management and nutrition for pregnant

Primary prevention in ECC management should be considered as prenatal and postnatal period. Because oral and dental health begins in the prenatal period and continues in the postnatal period. There is a relationship between oral health of mothers and ECC incidence in children (Nakai et al., 2010). It is seen that the incidence of ECC and Streptococcus mutans carriage in their children can be reduced when mothers are provided with education to support oral and dental health before birth (Xiao et al., 2019). For this reason, dental examination and education are necessary in the prenatal period in pregnancy (AAPD, 2021b). During pregnancy, it is recommended that women brush their teeth twice a day with fluoride toothpaste, in addition to floss daily and visit the dentist regularly. (Zou et al., 2022).

In addition, a balanced diet of mothers during pregnancy in terms of high-quality protein, vitamins, and trace elements is among the prenatal factors that affect the dental health of the child (Clarke et al., 2006). Prenatal and postnatal nutrition is important for enamel maturation (Takaoka et al., 2011). Enamel hypoplasia is more common in children with low birth weight and who have had a systemic disease in the neonatal period (Clarke et al., 2006, Takaoka et al., 2011). It has been proven that nutritional deficiencies in the perinatal period cause hypoplasia. There is also a consistent relationship between clinical hypoplasia and ECC, and therefore, healthy eating habits should start during pregnancy and continue for both mother and child in the postnatal period (Targino et al., 2011).

4.1.2. Breastfeeding and nutrition

Different feeding patterns made with breast milk, feeding bottles and infant formulas, sugary foods and beverages in infants can affect oral and dental health in different ways. Breastfeeding is a preferred and supported form of nutrition for the baby. Breast milk contains many chemical and cellular components such as carbohydrates, proteins, lipids, minerals, vitamins, growth factors and hormones, lymphocytes, macrophages, neutrophils, epithelial cells, stem cells and microRNA and It is emphasized that all components in breast milk have numerous functions such as providing growth and development in body cells, activating the immune system, showing anti-inflammatory and bacteriostatic effects, and aiding digestion (Gur et al., 2010).

The World Health Organization (WHO) recommends that babies should only take breast milk for the first 6 months, and that breastfeeding should be continued until 2 years of age and beyond after introducing complementary foods (White, 2008). The American Academy of Pediatric Dentistry (AAPD) has emphasized that breast milk is the most ideal food for babies, and provides general health benefits for both the baby, the mother and the society. When feeding with breast milk, it is emphasized that unlike the bottle, the milk does not circulate between the teeth, but is transmitted directly to the back of the soft palate. In addition, it is stated that during breastfeeding, the breast and nipple cause the baby's mouth volume to increase, creating a spontaneous swallowing reflex, and during bottle feeding, milk is kept in the mouth until the swallowing reflex occurs. Therefore, breastfeeding is reported to be the most successful option in terms of oral hygiene (Quadri et al., 2012). It is stated that breast milk is not cariogenic under normal feeding conditions, but causes the pH to decrease as the frequency and duration increase. Frequent feeding may increase the cariogenic potential, especially at night, due to decreased salivary flow rate during sleep (Nakayama et al., 2015; Tham et al., 2015). It has been stated that feeding the baby with breast milk for 7 or more times a day after 12

months may increase the risk of ECC (AAPD, 2005). Therefore, frequent and prolonged breastfeeding should be avoided during sleep when saliva flow is reduced. After each feeding, care should be taken to clean the teeth, and tooth surfaces should be wiped after night feeding.

Free sugar intake, which is the main cause of dental caries in children who switch to complementary feeding, should be limited to food and drinks, and feeding with a bottle of milk or drinks containing free sugar at night should be avoided. Young children should be encouraged to eat a diet high in fruits and vegetables and low in sugars, with different foods (Wright et al., 2014).

4.1.3. Fluoride Toothpastes

Fluoride plays a key role in reducing dental caries and its use is both safe and significantly effective for caries prevention and management (Schmoeckel et al., 2020). Low levels of fluoride in saliva and plaque help remineralize demineralized tooth enamel and prevent solid enamel from demineralization. It prevents caries with the mechanism of affecting the metabolic activities of cariogenic bacteria too (Riley et al., 2010). High levels of fluoride temporarily cause a calcium fluoride-like substance on the enamel surface. When the pH value drops as a result of acid formation, fluoride is released and is used to remineralize enamel as well as affect bacterial metabolism (Riley et al., 2010). Daily brushing habits with fluoride toothpastes play an important role in stopping ECC. Fluoride contributes to enamel remineralization and has a reducing effect on caries risk. Starting from the eruption of the first tooth, toothpaste with at least 1000 ppm fluoride, and tooth brushing habits should be maintained with age-appropriate amounts twice a day, and the primary prevention step for ECC should be maintained with adequate home care (Featherstone et al., 2021). The ADA and AAPD recommend a pea-sized amount of toothpaste for children aged 3-6 years and the amount of toothpaste in smear (approximately 0.25 mg F) in smear (approximately 0.1 mg F) up to age 3 years (ADA, 2014; Featherstone et al., 2021; Schmoeckel et al., 2020; Riley et al., 2010).

4.1.4. Dental visit

After the first tooth erupts, the first dental examination of babies should be done before the age of 1 year. Routine dental visits should be made every 3 to 6 months to check for bad mouth habits, caries, malocclusion, etc., including tooth development (Ramos-Gomes and NG, 2011). Early dental visits can minimize the occurrence of dental phobia by helping children adapt to the dental examination process and medical environment.

4.2. Seconder prevention

Secondary prevention in ECC is to prevent lesions before the cavitation stage or to promote remineralization (Urquhart et al., 2019). Early detection of incipient caries is extremely important in preventing cavitation. Secondary protection includes non-invasive measures including fluoride varnish applications for effective control of initial lesions before cavitation and pit and fissure sealant applications on sensitive molars (Pitts et al., 2019).

4.2.1. Fluoride varnish

Professional topical fluoride applications are effective in reducing and preventing dental caries. These treatments should be applied after the dental caries risk assessment is completed (Lenzi et al., 2016). The most commonly used substances for professional fluoride treatments are acidified phosphate fluoride and 5% sodium fluoride. The only professional topical fluoride material that can be used for children under the age of six is 5% sodium fluoride varnish. (Marinho et al., 2013). Sodium fluoride varnish should be applied by primary care teams to deciduous teeth or teeth with early signs of caries in children with ECC (WHO, 2019). Systematic reviews have reported that periodic application of 5% sodium fluoride varnish can stop initial caries in primary teeth, prevent the development of new caries, and help remineralize early enamel lesions (WHO, 2019; Marinho et al., 2013; Lenzi et al., 2016, Gao et al., 2016). Regular applications every three to six months are necessary for topical fluoride applications to remain effective (Weyant et al., 2013).

4.2.2. Casein fosfopeptit amorphous calcium phosphate (CPP-ACP)

Another agent used as a remineralization agent in the treatment of initial caries lesions is CPP-ACP (Cochrane et al., 2008). Casein is a phosphoprotein that makes up approximately 80% of milk protein (Reynolds, 2009). Casein phosphopeptide (CPP) contains the protein sequence of casein (-Ser(P)-Ser(P)-Glu-Glu) (Azarpazhooh et al., 2008; Çelik et al., 2011). CPP can stabilize calcium phosphate as a CPP-amorphous calcium phosphate (ACP) complex (Çetin et al., 2011). It has been reported in studies that the tryptic peptides of casein are included in the intraoral plaque and increase the quantity of calcium and phosphate in the plaque (Reynolds, 2006). The proposed anticariogenicity mechanism of casein phosphopeptide is colloidal calcium phosphate complexes, which increase the level of calcium phosphate in plaque, suppressing enamel demineralization and increasing remineralization (Rose, 2000). In the early stage, caries lesions are reversible as a result of diffusion of calcium and phosphate ions to the surface lesions and remineralization, and the lost structure is regained (Reynolds, 2006). CPP-stabilized calcium

phosphate ions are used to inhibit enamel demineralization and to promote remineralization (Elsayad et al., 2009). For any clinical application in the use of CPP-ACP in ECC, possible side effects from casein ingestion in people with Ig E allergy should be considered (Azarpazhooh and Limeback, 2008).

4.2.3. Pit and fissure sealants

Pit and fissure caries are an early disease process and when caries on the buccal and lingual surfaces are taken into account, more than half of caries in children and adolescents are pit and fissure caries (Juric, 2013). Due to the plaque retention of pits and fissures and the difficulty of cleaning, the incidence of caries on these surfaces is high (Kitchens, 2005).

Pit and fissure sealants have been a recommended procedure for primary and permanent molars to protect pits and fissures (Lam et al., 2020). Pit and fissure sealants reduce the formation of debris and plaque by acting as a physical barrier between tooth enamel and the oral environment, and are often used in caries management in conjunction with other preventive measures in patients at high caries risk (Nunn et al., 2000). Seal application is also used to prevent progression of initial caries in teeth with initial carious lesions and no cavitation (Innes and Manton, 2017).

4.3. Tertiary prevention

Tertiary prevention for ECC may include both non-invasive and preventive management for cavitated dentin lesions (Pitts et al., 2019).

4.3.1. Silver Diamine Fluoride (SDF)

Silver diamine fluoride (SDF) has recently become popular in stopping cavitation-causing lesions (AAPD, 2017). SDF is a colorless and alkaline solution consisting of diamine silver ion and fluoride ion (Timms et al., 2020). The effectiveness of SDF is formed by the combination of the antibacterial properties of silver ions and the anti-caries effects of fluoride ions, and was accepted as a caries stopper in the list of necessary medicines for children published by the World Health Organization (WHO) in 2021 (WHO, 2021). Silver (Ag) ions in SDF reduce the metabolic activity of *Streptococcus mutans* and inhibit its growth (Aksrapak, 2018).

Fluorine ions in SDF inhibit the progression of caries. The synergistic effects of silver and fluoride ions together provide the opportunity to stop the caries process and prevent the development of new caries lesion (Rosenblatt and Stanford, 2009). The American Academy of Pediatric Dentistry (AAPD) recommends the use of SDF for the treatment of caries in children, adolescents and including children with special health care needs (AAPD, 2018). According to the American Academy of Pediatric

Dentistry's (AAPD) silver diamine fluoride application guidelines, the indications for SDF are as follows:

1. Patients with lesions at high caries risk that will require more than one appointment
2. Patients with treatable caries lesion extending to the dentine in the anterior and posterior primary teeth
3. Active caries lesions with no clinical pulp involvement
4. Patients with behavioral problems needing dental treatment under general anesthesia
5. Patients with limited and no access to dental care
6. Patients with caries lesion in a position that can be reached with a micro brush for the application of SDF (Crystal and Marghalani, 2017).

4.3.2. Atraumatic restorative treatment (ART)

ART involves the removal of demineralized tissue with hand tools only, and is a minimally invasive approach characterized primarily by restoring the cavity with glass ionomer-based materials (Bridge et al., 2021). Glass ionomer cements are frequently used due to their sustained fluoride release and recharge, tissue biocompatibility and chemical bonding to dental tissues (Mandari et al., 2001). ART is a child-friendly approach that requires very little space preparation and does not require the injection of local anesthetic (WHO, 2019). It has been shown that ART has a high clinical success rate, particularly in single-surface restorations (De Amorim et al., 2012). ITR (interim therapeutic restoration) consists of the same technique as ART and it includes removal of carious tooth structures using hand or rotary instruments followed by restoration with glass ionomer cement or resin modified glass ionomer cement. Since the oral cariogenic bacteria levels can return to pre-treatment levels after six months in the ITR technique, the dental restoration is replaced with a more durable restoration within the next six months (Yip et al., 2001). The combined use of ART and the chemomechanical method has recently been frequently used in ECC treatment (Maragakis et al., 2001). The use of hand tools in combination with chemo-mechanical methods can increase the destruction of carious tissues and give better clinical results (Farag and Frencken, 2009). Silver modified atraumatic restorative therapy (SMART), which includes treatment of the caries lesion with SDF and then restoration with glass ionomer, is among the current treatment methods. This technique aims to effectively stop caries in the ECC without removing additional tooth structure. (Bridge et al., 2021).

4.3.3. Minimally invasive restorations

Restorative material selection should be done together with CRA in cavitated carious lesions. Glass ionomer cement and resin-modified glass ionomer cement may be preferred for occlusal, Class II, Class III, and Class V restorations in preschool children because these materials chemically bond to the tooth structure, release fluoride, prevent secondary caries, and help reduce the risk of caries (Schwendicke et al., 2016). However, due to the low mechanical properties of glass ionomer cements, they are not recommended for Class II restorations or incisal restorations of anterior teeth. Resin-based composite materials are frequently used for the treatment of occlusal, Class II, Class III and Class V restorations. Resin-based composites have stronger compressive strength and bond strength than glass ionomer cements. For this reason, they are preferred in restorations where mechanical forces are high (Giacaman et al., 2018).

4.3.4. Pediatric crowns

Composite prefabricated veneered stainless steel crowns, strip crowns, or prefabricated primary zirconia crowns have higher success rates in the restoration of teeth with a high risk of caries and excessive material loss due to caries (Walia et al., 2014). Thus, it can be ensured that the mesiodistal dimension of the primary teeth is preserved, the structural integrity of the tooth is preserved, it is biocompatible and the lifespan of the tooth is increased (Mulder et al., 2018).

The indications for the use of pediatric crowns in the pedodontic clinic can be listed as follows:

- Restoration of endodontically treated teeth
- Restoration of advanced interfacial caries
- Restoration of broken teeth
- Restoration of multiple caries
- In children treated under general anesthesia,
- In patients with bruxism,
- In the restoration of cervical caries lesions

It is used in the restoration of teeth undergoing pulpotomy-pulpectomy treatment (Mulder et al., 2018; Walia et al., 2014).

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CHAPTER 3

RATIONAL DRUG USE AND APPROACH OF DENTISTS TO RATIONAL DRUG USE IN TURKIYE

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Introduction

The pharmaceutical industry is a dynamic industry that is developing day by day. With the advancing technology, the development of medical treatments has also improved the pharmacology and enabled new drugs to be used. Increasing drug consumption with the ease of access to drugs has revealed the problem of effective and necessary use of drugs and the concept of rational drug use (RDU)(1). The negligence of rational drug use is a fundamental and important worldwide health problem that may pose a serious risk factor in the future. The use of drugs that are inconsistent with clinical findings, ineffective and economically irrational is a global problem that needs to be resolved (2). According to the data of the World Health Organization (WHO), more than half of the prescribed drugs are inappropriately prescribed and sold (3). Unnecessary prescription of antibiotics, which is one of the most widely used drug groups, easy access to antibiotics by patients, and non-medical uses increase resistance to diseases that we can treat with antibiotics. The development of resistance to antibiotics makes it difficult to achieve the desired success in treatment and negatively affects the country's economy (4). The use of unnecessary and incorrect doses of antibiotics in mild or advanced infections that arises both in the community and in the hospital environment prevents the appropriate treatment of diseases. Rationally applied correct antibiotic treatment increases the survival rate of the patients and it is beneficial in preventing complications, reducing the severity of the disease and the recovery period (5).

Rational Drug Use

Irrational use of drugs can lead to adverse scenarios with severe consequences. In order to prevent such situations, it is necessary to have sufficient knowledge about the rational use of drugs and then to be able to make the right applications. Rational drug use (RDU) is defined as “giving patients appropriate drugs in line with their clinical needs, in appropriate doses, for a sufficient period of time, at the least cost to themselves and to society”. The current definition of RDU is “drugs that meet the health care needs of the majority of the population and therefore should be available at all times in sufficient quantities and in appropriate dosage forms, and which can be afforded by society”. Inappropriate and unnecessary drug use has caused problems such as increased resistance to diseases, unwarrantedly consumption of resources and financial damage to the state treasury and these problems have made studies on rational drug use more important (6).

RDU steps can be sorted as: correct diagnosis, accurate determination of prognosis and survival, purpose of drug administration, evaluation of

alternative treatment options, correct prescription of necessary drug in appropriate doses. It is essential to be sure of the necessity of the drug, to analyze the effectiveness and safety of the drugs, to provide correct guidance and patient participation in all steps (7). RDU has three main elements: supply (physicians, pharmacists, industry), demand (patients) and control mechanisms (state, civil society organizations) (8).

a. Supply element (physicians, pharmacists, industry)

Physicians, who form the basis of the first element, play an important role in rational drug use. Indications, patient characteristics, attitudes of physician and even the infrastructure of the institution where the prescription is written can be important especially in prescribing antimicrobials, which have an important place in medicine and dentistry. Factors such as physicians' drug knowledge, correct indication and the quality of the education given at are important for the applicability of rational drug use (9).

Uysal et al. evaluated the rational drug use of physicians according to their drug knowledge and years of professional experience, and it was determined that dentists who have just graduated or in their first ten years in the profession still remember the information they received at the college and have sufficient knowledge about rational drug use in the current literature. However, it has been learned that physicians who have worked for many years are stick to the prescription that they are used to or consult new physicians. In addition, only 11.3% of the dentists included in the study stated that they knew the pharmacokinetic and pharmacodynamic properties of the drugs and it was learned that 20% of the general dentists did not receive anamnesis from the patients. Also it was learned that very few physicians gave information about the use of drugs to patients (10).

Koyuncuoğlu et al. reported that the rate of prescribed drugs within a year was 39.4% and the rate of antibiotics among prescribed drugs was 56.8% (11). In order to reduce these values, physicians should have accurate information about indication and patients should be directed to rational drug use. Çanakçı et al. reported the rate of antibiotics prescribed in oral and dental health hospitals as 51% and the rate of antibiotic requirement as only 9% as a result of the clinical examination performed in school of dentistry (12). One of the main reasons for this situation may be that specialist dentists in school of dentistry providing tertiary care dental treatments have a higher level of knowledge than general dentists. Serçe et al. stated that physicians working in the faculty hospitals could spend more time for patient examination and therefore prescribed less medication than physicians working in the family practice center (13).

b. Demand Element (Patients)

Patients, who constitute the second important element of drug prescribing, are also of great importance in the pharmaceutical industry. The supply-demand relationship that develops between physicians or pharmacists and patients, and patients' insufficient level of knowledge about drug use put on the line the principles of rational drug use (8,13). Çanakçı et al. stated that 45% of the patients who applied to their family practice center due to dental pain and requested antibiotics, but only 8% of these patients who applied to the faculty hospital required antibiotic treatment. In addition, 58% of these prescriptions were given upon the request of the physician and 11% upon the request of the patient (12).

Gül et al. stated that more than half of the patients applied to a health institution for any reason and requested antibiotics, and 6.4% of the physicians prescribed antibiotics to these patients (14). In the study of Çöplü et al., this rate was found to be 17% (15).

According to the studies in the current literature, antibiotics are widely used incorrectly despite the strategies developed in today's Türkiye. According to the one research, 151 of 203 patients were misdiagnosed and used antibiotics even though they were not indicated. Although there is irrational use of antibiotics around the world, the high rates in our country compared to developed countries creates a major problem (16,17).

The medicines given by the physicians with the correct diagnosis should be used appropriately by the patients and the instructions given by the physician should be taken into account by the patients. In a study, it was learned that patients did not use the prescribed drugs for the recommended duration and doses, they took the drugs until their complaints subsided and then stopped taking them (3). In addition, it is a well-known fact that patients can take drugs directly without a prescription and stock these drugs at home. It has been determined that the only parameter that patients pay attention to for home-stocked drugs is the expiration date (ED) and drugs that do not beyond ED are used without consulting the physician. The amount of home-stocked medicine was reported as 93.7% by Bayberk et al, 88.4% by Göçgelidi et al. and 83.1% by Muras et al. (18-20).

c. Control Mechanisms (State, civil society organizations)

According to WHO data, the rate of insufficient education and inappropriate antibiotic use is reported as 45-90% worldwide, while this rate has been reported as 40-60% in our country (21). In a study conducted in Turkey in 2003, the rate of drug expenditures in the total health-care costs of social security institutions was found to be between 45-50% (22). These rates revealed the necessity of control mechanisms. "The Essential

Guide to Prescription Drugs” edited by WHO in 2003 was translated into Turkish and “The Diagnostic and Treatment Guides for Primary Care” prepared by the School of Hıfzısıhha have been published. Due to the lack of progress in the rational drug use during this period, the Rational Drug Use Branch Office was founded in 2010 and the Türkiye Pharmaceuticals and Medical Devices Agency was founded in 2011. Since 2010, the Ministry of Health has started to take measures such as the “Drug Tracking System” and data matrix application and also developed strategies that will serve as a bridge between physicians and pharmacists, such as checking the antibiotic list in the pharmacy, regular feedback of laboratory results, regular control of antibiotic request forms and written prescriptions (4.23). It was aimed to educate physicians on RDU, to keep up with the current literature and to increase the awareness of patients in terms of conscious drug use with these implemented health policies (24).

Rational and Irrational Use of Antibiotics

Since the most orofacial infections are odontogenic origin, dentists routinely prescribe antibiotics to treat infections. The physician who will administer the antibiotic treatment should have knowledge about the pharmacological properties of the drug, know the antibiotic sensitivity of the causative microorganism before prescribing the drug and have sufficient information about the severity of current infection and the patient profile. Prescribing and using antibiotics in line with these informations is called rational antibiotic use (RAU).

When it comes to oral flora in dentistry, routine antimicrobial susceptibility tests are very important for the infection agent and its isolation. Although empirical treatments are generally sufficient for dental infections, the inability to perform routine tests negatively affects the radical treatment and leads to a tendency towards broad-spectrum antibiotics (9,25). A study has shown that most of the physicians prefer penicillin derivated, broad-spectrum antibiotic combinations such as amoxicillin + clavulanic acid for dental infections. However, it is known that the use of narrow-spectrum preparations provides less changes in the oral flora and reduces the risk of developing superinfection (26). In accordance with the principles of AAK, the physician should prescribe the appropriate antibiotic for the required time and dose and explain the appropriate use of the drug to the patient. The patient’s drug use regimen should also be followed-up.

Antibiotic therapy should be prescribed to support dental treatment and should never be considered the only treatment modality. Antibiotics should be given to the patient in infections accompanied by systemic symptoms (fever, weakness, fatigue, lymphadenopathy and trismus) or

in conditions such as abscess/cellulitis where the infection is at risk of spreading and antibiotics should not be prescribed only for pain or swelling (27). In cases where these criteria are not met, the use of drugs is called Irrational Drug Use (IDU) and the use of antibiotics under inappropriate indication is called Irrational Antibiotic Use (IAU). (28).

Irrational drug use causes a decrease in the response of patients to treatment and therefore an increase in morbidity and mortality. In addition, it can cause adverse conditions such as development of resistance to antimicrobials, drug reactions, decrease in patient compliance with treatment and damage to the country's economy. The financial aspect of AOİK also constitutes an important part of the issue. Unnecessary expenditures due to drug use negatively affect the country's economy but also pose a risk to public health. If current drug use habits continue, it can be foreseen that more serious conditions will be encountered in the near future in addition to current problems. Long or short-term use of antibiotics than necessary, antibiotic preference that does not meet the indication criteria, out of need and prophylactic use of antibiotics, preference of broad-spectrum antibiotics, inappropriate use of antibiotics in patients with special systemic conditions such as the elderly, child or pregnant contribute this prediction. In addition, unconscious stocks will prevent access to medicines in case of need (28,29).

For all these reasons, research on RDU are carried out and health policies are made all over the world. Drug reactions that may be seen in future generations or the occurrence of infections that cannot be treated in the future due to the development of antibiotic resistance, although they can be treated currently, emphasize the importance of RDU. Within the framework of the principles of RDU, prescribing the most appropriate antibiotics to the patients in the required dose and time, according to the clinical needs of the patients and supervising the patient's antibiotic use are among the basic responsibilities of the dentists. So with this awareness, the dentist takes an important responsibility before the prescription is written and the patient takes it after. Patients should also pay attention to the doctor's instructions and stay away from inconsistent behaviors. In order to achieve this, educations on the RDU should be organized in our country and also the worldwide and they should be accessible for everyone.

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CHAPTER 4

DIGITAL DENTISTRY

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DIGITAL DENTISTRY

Technology advancements have accelerated the digitalization of dentistry. In many dental fields, digital patterns are used. One of the highlights of recent times has been the conversion of data from intraoral scanners into digital models, and then modeling using various manufacturing techniques. Every clinician should keep up to date on the topics of intraoral scanners, CAD-CAM systems, and 3D printers, which are the cornerstones of digital dentistry.

CAD-CAM in dentistry was introduced in the 1970s, and two researchers named Duret and Preston used the first dental CAD-CAM system (Duret & Preston, 1991). CAD-CAM systems basically consist of 3 stages: The first is the collection of data by scanning the preparation intraoral or extraoral. Then the CAD system, that is, the three-dimensional design of the restoration on the computer, and the final stage is the production of the restoration, the CAM stage (Çelik, Tuğrul, & Üşümez, 2013). CAD-CAM systems consist of optical scanner, software (CAD) and hardware (CAM) that creates the design (KALAYCI & BAYINDIR, 2015). Optical scanners are based on the principle of obtaining images of three-dimensional structures, which is defined as the triangulation procedure. The design software performs the three-dimensional design and planning of the restoration on the computer screen. The user can use the templates in the software or make his own design (KALAYCI & BAYINDIR, 2015). The last component, CAM, refers to the milling machines under the control of the computer, while the restoration is obtained by milling from the material blocks, some manual arrangements (polishing, coloring, porcelain applications, etc.) are completed by the dental technician as the final stage (KALAYCI & BAYINDIR, 2015; Tinscherta, Nattb, Hassenpflugb, & Spiekermann, 2004).

Currently, it is possible to demonstrate that additive technologies can replace subtractive ones. The 3D printer was created by Charles Hull, who first revealed it to the scientific community in 1980 and cemented its historical significance with his stereolithographic printing patent filing in 1986 (Kessler, Hickel, & Reymus, 2020). Although the patent granted stops the development of new technologies for a considerable amount of time, 3D printers have developed quickly and are still developing (Kessler et al., 2020).

INTRAORAL SCANNER SYSTEMS

Today, the number of both devices and manufacturers used in CAD-CAM systems is increasing day by day. Digital systems have been developing very rapidly in recent years. Many companies are introducing their intraoral scanners to the dental industry. Newly developed scanners are the subject

of numerous studies on digital scans. Therefore, it is important for users to keep their information about browsers up-to-date (BAKIÇ, KOCACIKLI, & KORKMAZ, 2021). The concepts of “precision and accuracy” in the measurements made by the scanners are directly related to the quality of the digital measurement obtained. While the precision of a scanner describes its closeness to the measurement values, the accuracy in scanners describes the success level of the measurement or how close the measurement is to the true value. The accuracy of a scanner is the difference between the true value in measuring a physical property and the value the model indicates. According to the standard, the closeness of accuracy and precision affects the quality of the measurement (Accuracy, 1994; BAKIÇ et al., 2021).

For restorative dentistry, there are currently more than ten intraoral scanning devices (Logozzo, Zanetti, Franceschini, Kilpelä, & Mäkynen, 2014). As of now, there are several types of intraoral scanners available. These scanners are made to collect data using imaging technologies like parallel confocal laser scanning, triangular scanning, optical coherence tomography, active wavefront method, accordion fringe interferometry method, near infrared imaging technology, and structural light imaging technique (BAKIÇ et al., 2021).

Current Intraoral Scanners

CEREC Sirona Dental System GmbH (Germany)

The CEREC 1 system (Sirona, Bensheim, Germany) was launched in 1987 as a digital measurement and CAD / CAM device, together with the Duret system (Rekow, 2006). This system is designed with the concept of “triangulation of light”, in which the intersection point of three linear light beams is focused on a specific point in three-dimensional space (Moörmann, 2006). The visible blue light that an LED light source emits is used by the CEREC AC Bluecam device to take pictures. One quarter of the mandible can be digitally measured by CEREC AC Bluecam in under a minute, and the opposing quarter can be done in a matter of seconds (Medina-Sotomayor, Pascual-Moscardo, & Camps, 2019). In 2012 [12], CEREC AC Omnicam was introduced. A three-dimensional model is produced by the Omnicam imaging method, which employs video scanning technology and continuously photographed images (Ting-shu & Jian, 2015). Omnicam imaging technique uses video scanning technique and continuously photographed images create a three-dimensional model (Medina-Sotomayor et al., 2019). Bluecam can only be used for one tooth or quadrant, whereas Omnicam can be applied to a single tooth, quadrant, or complete arch. The exceptional characteristics of Omnicam include its color 3D images and powder-free scanning. (Birnbaum, Aaronson, Stevens, & Cohen, 2009).

Lava C.O.S. System

Lava C.O.S. It is an intraoral digital scanner invented in 2006 and released in 2008. It works under the active wavefront principle (Rohaly, Hart, & Brukilacchio, 2008). A trio of sensors can simultaneously take clinical pictures from various angles, and using their own image processing algorithms, they can create surface pictures with in-focus and out-of-focus information. (COS, 2009). Lava C.O.S. It has the smallest scanner tip and is only 13.2mm wide. The scanner sends pulsed visible blue light as the light source and works with a mobile host and a touchscreen (Galhano, Pellizzer, & Mazaro, 2012). Lava C.O.S., which is similar to CEREC AC Bluecam, also calls for covering the tooth surface with a grainy powder prior to scanning. A specific powder is sprayed onto the tooth surface to create a uniform covering after rinsing and air-drying. (Birnbaum et al., 2009). Dentists can quickly determine whether they are receiving enough info from the preparation with real-time visibility. (Birnbaum et al., 2009).

iTero System

Cadent Corporation (Carstadt, NJ) introduced iTero in 2007. Based on the concept of parallel confocal imaging, the iTero system uses laser and optical scanning to record intraoral surfaces and contours. (Garg, 2008). Only with iTero system, parallel confocal scanning could catch all components in the mouth without covering the teeth with powder (Galhano et al., 2012). The computer system, a mouse, a keyboard, a display, and a scanner are all elements of this system, which uses a red laser as its light source. (Birnbaum & Aaronson, 2008).

E4D System

D4D Technologies, LLC (Richardson, TX) created the E4D device using the concepts of optical coherence tomography and confocal microscopy. Its light source is a crimson laser. The proximal teeth and prepared tooth are digitally captured by the E4D's high-speed laser to produce an interactive three-dimensional picture. (Logozzo et al., 2011). Images are taken using laser technology from all directions. The software generates an image library. This technology can also be used as an intraoral scanner without the use of powder. (Ting-shu & Jian, 2015).

TRIOS System

A new intraoral scanner system called TRIOS was introduced in 2011 by 3Shape (Copenhagen, Denmark), in 2010. This technology operates on the basis of confocal microscopy and ultra-fast optical sectioning. The system maintains a fixed spatial relationship between the scanner and the scanned item while recognizing changes in focal plane location. (Logozzo et al., 2011). Trios 3 (Cara Trios) is a scanner produced by 3SHAPE A/S

and is frequently used today. Trios 3 was released in 2015. They are available in the form of a pencil holder or in the form of a pistol. 3shape launched wireless scanner models in 2017(Mangano et al., 2019). Trios 4, on the other hand, has a new smart type of transillumination imaging feature. This system includes infrared rays. In this way, it helps to identify invisible proximal caries. However, its use has not been approved by the FDA and its clinical use is not currently available(BAKIÇ et al., 2021). Intraoral scanners, which open the doors of digital dentistry and enable us to obtain models in the computer environment, have various technological infrastructures and features. The success of scanner systems is increasing day by day thanks to the curiosity and studies of researchers on the subject.

CAD-CAM SYSTEMS

According to Production Methods:

1. Systems Applied Directly in the Clinic
2. Systems Used in the Laboratory
3. Production Centered CAD-CAM Systems

analyzed under three headings.

1.Systems Applied Directly in the Clinic:

CEREC

Sirona (Sirona Dental Systems GmbH,Benshelm,Germany) is the only manufacturer with systems that can produce both in the clinic and in the laboratory. It is the first produced CAD-CAM system. The first produced CEREC system was released in 1985 and the latest version is SW CEREC 4.2.4. It was launched in 2014(KALAYCI & BAYINDIR, 2015). In the first CEREC systems, poor marginal fit and failures in shaping the occlusal surface were overcome with CEREC 2, whereas restorations with CEREC 3 had a high success rate(Christensen, 2001; ÇETİNDAG & Ayşef, 2016).

EVOLUTION 4D DENTIST

Intraoral scanning can be performed without the use of reflective powder in the E4D Dentist system, which was launched in 2005. The image taken from many angles is converted into data points and the software can generate the correct morphology on the computer. With the ICEEverything View software, the differentiation of soft and hard tissue, the periphery of the crowns and the clarity of the oral environment can be seen in the 3D image. With the “autogenesis” feature of the device, a personal design compatible with anatomical structures is made (Çelik et al., 2013).

2. Systems Used in the Laboratory:

In these systems, scanning is made from a plaster model or measurement. After the infrastructure is produced, the technician applies porcelain over the restoration(KALAYCI & BAYINDIR, 2015).

CEREC inLab

It was produced in 2004. The digital measurement of the model is taken with the scanner (inEos Blue). inEos Blue part of the system; scanner, computer and inLab 3D scanner-design software. Apart from the InEos Blue part, there is also a milling and sintering device in the system. With the “biogeneric” feature of the software, restoration can be performed with a morphology similar to the existing teeth of the patient(Çelik et al., 2013).

CERCON

It was launched in 2002. The manufacturer company first became a CAD/CAM system after adding a three-dimensional optical scanner (Cercon eye) and Cercon Art CAD design software to the system in 2005, only as a CAM system. During the scanning process, restorations can be scanned with an accuracy of 10 microns in less than 20 seconds (KALAYCI & BAYINDIR, 2015).

3. Production Centered CAD-CAM Systems

After the model is scanned, data is collected, sent to the main hub via the internet, and the designed repair is sent back to the lab for finishing touches.

LAVA

It was released in 2002 by 3M ESPE(Çelik et al., 2013). The Lava system consists of an optical scanner (Lava Scan), a computer-aided milling machine (Lava Form), a furnace for sintering (Lava Therm) and CAD/CAM software (Palin & Burke, 2005). After the measurement is taken, the model is scanned with the scanner, the data is transferred to the computer, and the infrastructure is created. Since it will shrink during the sintering process, the milling process is carried out by enlarging the design between 20-25% (Piwowarczyk, Ottl, Lauer, & Kuretzky, 2005).

PROCERA

In 1993, the Procera All Ceram system was developed in collaboration with Nobel Biocare and Sandvik Hard Materials (Andersson, Razzoog, Odén, Hegenbarth, & Lang, 1998). The design infrastructures of the Procera system are available in the laboratories, but the production units are only in Sweden and the USA. Scanned models are sent to Nobel Biocare Sandvik on the internet (Boening, Wolf, Schmidt, Kästner, & Walter, 2000; Hager, Odén, Andersson, & Andersson, 2001).

THREE DIMENSIONAL PRINTERS (3D PRINTER)

The phrase “3D printing” is frequently used to refer to a manufacturing process that builds up layers of an item one at a time. Rapid prototyping is another name for this technique that more correctly describes it (Andonović & Vrtanoski, 2010; Liu, Leu, & Schmitt, 2006).

The model production process in 3D printers starts with the transfer of the model obtained from the measurement taken from the patient or the digital measurement taken to the CAD software with the stl extension. The digital model is sliced into layers after the necessary supporting structures are designed in software. The segmented data is routed to the printer and the material is poured in layers in the printer. In the last stage, the supporting structures are removed from the 3D models obtained from the printer, and they are passed in sandblasting-washing-milling processes. Metal objects are heat treated after leaching (Dawood, Marti, Sauret-Jackson, & Darwood, 2015).

3D Printing Technologies and Materials Used:

1. Technologies using light-cured resin
 - a) Stereolithography (SLA)
 - b) Photojet PPJ (Photosensitive polymer spray)
 - c) DLP (digital light processing)
2. Powder-dependent technologies
3. Technologies working with sintered powder
4. Technologies using thermoplastic

1. Technologies using light-cured resin:

a) Stereolithography SLA: Stereolithography (SLA) is the oldest and most commonly used 3D printing method in dentistry. Production takes place by immersing a platform that moves from the top down or from the bottom up into the reservoir containing liquid monomer. The cycle is repeated for each layer until the desired object is created (Kessler et al., 2020).

b) Photojet (Photo-sensitive polymer spraying): In photopolymer spraying processes, the object is formed in layers by several linear heads. Objects with various colors and gradients can be created by using more than one title (Hofmann, 2014).

c) DLP (digital light processing): DLP technology includes a micro-system with a rectangular mirror arrangement called a digital micro-mirror device (Kessler et al., 2020).

2. Powder dependent technologies:

It is a variation of the photopolymer spraying process and involves applying an adhesive in powder form using pressurized nozzles(Kessler et al., 2020).

3. Technologies powered by sintered powder (SLS):

Selective laser melting is an insertion technique that uses heat generated by computer-controlled laser radiation to selectively and sequentially strengthen layers of powder material one after another, creating 3D parts(Xu, Wong, & Loh, 2001).

4. Technologies using thermoplastics (FDM):

The modeling technique made with molten material was developed by the founder of Stratasys more than 20 years ago and is protected under the trade name “fused deposition modeling” (Kessler et al., 2020). The 3D printer instantly fuses layers of molten plastic, creating very complex parts that are easy to manufacture. The finished object can be used in combination with various materials such as acrylic or wax(Dawood et al., 2015; Zaharia et al., 2017).

DIGITAL SMILE DESIGN

Digital smile design is an idea that seeks to help the clinician by enhancing the aesthetic visualization of the patient’s concern, offering a knowledge of the potential solution, and educating and inspiring them about the advantages of treatment. This will increase case acceptance. Patients take part in the process of creating their own smile using a digital image.(Coachman, Yoshinaga, Calamita, & Sesma, 2014).

Ackerman et al. from 2002, which introduced digital smile analysis and design, also includes the dynamic analysis of a smile using videography(Ackerman & Ackerman, 2002). Instead of making aesthetic reference marks on printed photos or plaster models, clinicians and technicians can now use the computer applications PowerPoint, Keynote, and Photoshop to do so on patients’ computer screen portraits of their faces and smiles(McLaren & Culp, 2013). In the mid-2000s, a number of computer programs were created to streamline these procedures and project idealized and reversible tooth proportions and shapes onto a digital picture (Zimmermann & Mehl, 2015). With the help of a number of facial, extraoral, and intraoral photographs, the first completely face-oriented digital smile design protocol was created in 2008 (Coachman, Calamita, & Sesma, 2017). The creation of the by fusing 2D images with 3D computer models. Several computer programs were created in the mid-2000s to streamline these procedures as well as to cast idealized and customizable

tooth proportions and shapes onto a digital picture. (Zimmermann & Mehl, 2015). In 2008, the first fully face-oriented digital smile design protocol was developed with a series of facial, extraoral and intraoral photographs (Coachman et al., 2017). Combining 2D photographs with 3D digital models has led to the transition to an all-digital format to validate and enhance aesthetic parameters in 3D (Coachman & Paravina, 2016).

Digital tools already used in dental practices today, such as a computer running DSD software, a digital SLR camera, or even a smartphone, are used to carry out the digital smile design (DSD) method (Daher, Ardu, Vjero, & Krejci, 2018). Additional instruments for a full digital 3D workflow include a digital intraoral scanner, 3D printer, and CAD/CAM for digital impressions (Aragón, Pontes, Bichara, Flores-Mir, & Normando, 2016).

DIGITAL SMILE DESIGN SOFTWARE

1. Photoshop CS6 (Helvey, 2007a, 2007b; McLaren & Culp, 2013) and **Keynote**(Coachman, Calamita, & Ricci, 2018; Meereis et al., 2016), all facial, dentogingival and dental aesthetics, thanks to the practitioner's ability to process any photograph (frontal, lateral, occlusal, retracted, etc.) and freely draw reference lines and angles can analyze the parameters. Keynote can analyze all parameters, but not change tooth characterization (Coachman & Calamita, 2012; Coachman et al., 2018; Coachman et al., 2012).

2. Aesthetic Digital Smile Design (ADSD) program, its working interface has been prepared in this manner because Valerio Bini specifically designed it for digital smile design. Less technical knowledge is needed to use the software successfully, but the functions are restricted to those offered by the program. The ADSD software was developed with the intention of carefully analyzing and digitally simulating a smile. It takes into account facial, dentogingival, and dental parameters. To make a digital wax model, it can be connected to a CAD/CAM system(Bini, 2014).

3. Cerec Smile Design is a software tool incorporated into Cerec Chairside software (since version 4.2) and inLab software (since version 4.2). In during CAD design process, the Cerec Smile Design tool can be triggered from the toolbar. As a result, attractive anterior restorations can be directly designed in 3D. One aspect of this technology is the BioCopy CAD design mode. In this method, a mock-up can be scanned directly intraorally and used as a 1:1 reference guide to design the completed restoration.(Santos et al., 2017). To manage all aspects of digitally designed restorations, including functional evaluation of the models' articulation, Cerec SW 4.2 can create a 3D digital model of the patient's face. (Allen, Schenkel, & Estafan, 2004; Perez-Davidi, 2015).

4. DSDapp is developed by a researcher who has published studies on the use of Keynote for digital smile design (Coachman et al., 2018; Coachman et al., 2012). By defining baselines, analyzing dentofacial features and proportions, and analyzing the connection between teeth, lips, and gingival tissues all within the application, DSDapp helps users to perform these tasks. In the initial clinical session, the patient was able to picture the case's narrative. It is challenging to complete during the same clinical session with patient involvement when using conventional DSD on a computer because it takes more time to prepare. (Omar & Duarte, 2018). DSDapp also uses the concept of Visagism. Dr. This concept, introduced by Braulio Paolucci, interprets smile design according to personality traits.

5. VisagiSMile is a program developed entirely on the concept of Visagism (Feraru, Musella, & Bichacho, 2016; Iliev, 2016). The software's goal is to present a revolutionary technology involving the development of a personalized personal image that conveys an individual's sense of self. VisagiSMile is a multiplatform web application for cosmetic dentistry that can be accessed immediately after completing a brief registration procedure. In order to enable dentists to work on various hardware platforms, including computers, tablets, and cellphones, all cases and data are kept on a server. (Yankov et al., 2016).

6. Planmeca Romexis smile design (PRSD): The 2015-released Planmeca Romexis Smile Design software, which allows smile design in a moment, runs on Windows and MacOS without the need for any additional supporting software. In the software, which includes VITA Classical and VITA 3D-Master tooth colors (Vita) in its library, a Color Picker tool can identify existing tooth colors and collaborate with virtual diagnostic wax up (Zimmermann & Mehl, 2015).

7. Smilecloud: The intraoral scanners (STL) or cone beam computed tomography scanners (CBCT) and images of patients can all be stored on the new cloud-based technology platform known as Smile Cloud. After the required loading is completed, artificial intelligence identifies and positions the teeth's proper shape. (Chen, Stanley, & Att, 2020).

8. Smile Designer App: The "Smile Design Algorithm" technique is used by the Smile Designer App, a web-based digital smile design software. It has been reported that this software can export PNG images of smile designs for use with all CAD/CAM systems, and that 3D printers can print pre-designed STL outputs of tooth models. (US, YÜZBAŞIOĞLU, ALBAYRAK, & ÖZDEMİR, 2021).

9. Smile Designer Pro: This digital smile design program, specially designed for use in dentistry, needs additional photos in addition to the front face smile photo (Omar & Duarte, 2018; Zimmermann & Mehl, 2015).

10. Exocad Smile Creator: Existing patient photos or webcam photos are quickly transformed into 3D objects by Smile Creator, which is integrated into the Chairside CAD software, then coordinated with 3D scans of the dentition. (US et al., 2021).

11. Digital Smile System (DSS): There are two different versions of the independent software program known as the Digital Smile System (DSS) (Easy and Pro). With reference points for exact reproduction of proportions, full-face photographs can be captured from the front while the patient is wearing special glasses. The only images that can be used to compare with the virtual system are screenshots of 3D models. Nine prefabricated templates with various surface profiles are included in the system, and it can also incorporate extra tooth libraries. (Zimmermann & Mehl, 2015).

CONCLUSION

Digitalization in dentistry is gaining momentum day by day. In the near future, being able to provide the fastest and most successful treatment to patient demands will depend on closely following digital dentistry. The interfaces of current CAD/CAM software solutions must be developed to enable changes between 3D diagnostics, 3D design, and 3D treatment in order to accomplish a treatment. The possibility of virtual therapy planning followed by digital-only treatment seems doable and promising in light of recent advancements in CAD/CAM technology. The initial step in this approach can be virtual smile design. The interfaces of current CAD/CAM software solutions must be developed to enable changes between 3D diagnostics, 3D design, and 3D treatment in order to accomplish a treatment.

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CHAPTER 5

DIGITAL SOLUTIONS FOR INDIRECT RESTORATIONS

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DIGITAL SOLUTIONS FOR INDIRECT RESTORATIONS

Conventional dental practices have begun to be shelved, just like in any industry that tries to keep up with the rapidly developing and digitalizing world. In recent years, the field of dentistry has experienced many advancements, with the use of digital technology playing a significant role in many of these changes. Digital dentistry is the practice of using computer and digital technologies in dentistry. These innovations increase the effectiveness, precision, and minimally invasiveness of dental treatment.

The methods that can be saved and modified in a computer environment, as well as those for early caries detection, have replaced the conventional methods in restorative treatments, providing more preventive and minimally invasive treatment options.(Peng, 2021) Additionally, traditional dental caries have been measured using intraoral and extraoral scanners. Methods started to replace them. Dental professionals can use these scanners to create a digital model of the teeth and gums by scanning them in 3D. Using CAD/CAM systems, these digital models can be used for fabrication and design of restoration projects.(Kaleli, 2021) The use of these new technologies can have a significant positive impact on patients as well as dentists. As digital scanning and design processes are used, for instance, time and money are saved. Additionally, using digital models reduced treatment times and increased the precision and beauty of restorations. Additionally, the expanding product variety allows for the creation of restorations tailored to each case, the recording of joint movements, and the achievement of more aesthetically pleasing results, all of which contribute to high patient and dentist satisfaction. As a result, digital treatments have a lower chance of failing, mismatching, and restoring restoration.(Coachman, 2021), (Peşkersoy, 2022)

DIGITAL IMPRESSIONS

One of the most important stages of restorative treatments in dentistry is the impression stage. 3D scanning of the mouth and teeth has gained importance in restorative, prosthetic, and orthodontics. In the 3D mapping of the oral cavity, a digital impression of the mouth is intended to be produced. For indirect restorations, it is extremely important to record all the details of the prepared cavity, the relations with the adjacent teeth in contact, and the patient's occlusion, obviously and accurately.(Naumovski, 2017) Three-dimensional scanners are used in dentistry; They can be classified into two main groups as intraoral and extraoral. These systems provide computer-aided recordings in dentistry. The digital systems used have advantages over traditional measurement systems. Digital systems have been developed very rapidly in recent years. Many companies are

introducing intraoral cameras to the dental industry. Recently released cameras and the best camera models currently in use lead the way in numerous areas built around digital scans. For this reason, companies need to keep them updated to protect their users. The impression materials and methods that have been used in dentistry for years have problems such as deformation, distortion, and inadequate adaptation. (Naumovski, 2017) Errors such as the inability to create details, especially in deep cavities and perplexed teeth, or insufficient and incompleteness in areas close to the gingiva are also encountered. (Pandey, 2019) Silicone impression materials were developed for this purpose. Although undesirable side effects due to the material have been reduced, errors may occur in the exact determination of the details of the soft tissues and the closure. (Kihara, 2020) The success of the restoration is directly proportional to the clarity of its dimensions. Dentists should consider possible defects in the cavity or preparation such as undercuts, sharp edges, and corners. It is critically important to realize it at the stage of ü. “Intraoral Digital Scanners”, which have been developed since the 2000s, have provided a lot of convenience to dentists. (Liu, 2014) The first produced scanners did not gain enough popularity due to the reasons such as using powder to determine the cavity boundaries, being low resolution, and black-white images. (Amornvit, 2021) Scanner technology, which has developed in the last 10 years, has advanced to a level that provides both ease of use and accurate and reliable measurement. In modern intraoral scanners, color photographs of teeth and soft tissues are taken from many different angles, and 2D photos are converted into 3D meshes by combining them with the software in the system. (Güth, 2017)

Studies comparing digital impressions with traditional polyvinyl and polyether materials have shown that deformation and distortion are significantly reduced in digital methods. They are effective in eliminating the restoration-tooth mismatch because they provide restoration. (Revilla-León, 2021) Most of the intraoral scanners available for use in today’s dentistry are open source and allow production in different CAD/CAM units. provides resources (Table-1). However, scanner units of CAD/CAM units with closed software programs such as CEREC only use files that can be transferred and used for their own devices and software. The main purpose here is to prevent the loss of resolution that the image may experience when converting it to different formats. The software of intraoral scanners such as Trios (3Shape, USA) and Primescan (CEREC, USA) also offers the option to set a color shade after scanning. (Akl MA, 2022)

Table 1 Intraoral Scanners Used in Dentistry

Intraoral scanner	Scanning Accuracy	Open source	Output Format	Scanner Type	Other Features
CS 3600 (Carestream, ABD)	9.8 micron	YES	DCM, STL, PLY	Structured light	Device with smallest scanner instrument, Color scanning, Control from tablet.
CARES (Straumann, Germany)	20 micron	YES	STL	LED Projection	Voice and gesture control, smallest scanner head, full mouth scanning feature thanks to its 5 cameras.
TRIOS (3Shape, Denmark)	<5 micron	YES	DCM, STL	3D Video, Confocalmicroscopy	Real color scanning, HD photo recording, Tooth color selection, 3 seconds closing.
Medit I700	10 micron	YES	DCM, STL	Structured light, Active Speed 3D Video™Video™	True color scanning, AI-powered margin Line Creation, Scan replay function
CERECsAC-Bluecam Sirona Dental System GMBH (DE)	-	NO	Proprietary	Active triangulation and confocal microscopy	Necessity of coating with titanium dioxide, Multiple imaging, Blue light source
Omicam (Cerec, USA)	5-6 micron	NO	STL, DCM	Structured light-Optical triangulation and confocal microscopy	Natural tooth color scanning, 3D video recording, Color selection, Minimum distortion.
iTero (Align Tech, Sweden)	12 micron	YES	STL	Parallel confocal microscopy	Comparison on dental records, Color and fast scanning, Orthodontic movement planning.
Planmeca Emerald (E4D Tech, USA)	<5 micron	YES	STL, PYZ, XML, D4D	Laser	Fastest scanning in single tooth restorations, Tooth color selection, automatic closing feature
True Definition (3M ESPE, USA)	<5 micron	NO	STL	3D Video	Unlimited cloud support, free software upgrades, detachable from CAM unit.

COMPUTER AIDED RESTORATIONS (CAD/CAM)

With CAD/Cam technology, faster, safer, and more successful applications can be made in many areas of dentistry today. In recent years, In recent years, CAD/CAM technology, which was first mentioned in the 80s, has been used more in dental clinics and laboratories. (Beuer, 2008) The main advantage of CAD/CAM technology is the high quality of the materials used and low production costs. However, treatments can be completed on the chairside to increase patient comfort and shorten

the treatment process. In multiple productions, support can be obtained from dental laboratories. In CAD/CAM chairside systems, as the dentist designs the restorations the dentist designs the restorations and case-specific conditions can be carefully evaluated and planned. (Davidowitz, 2011) There are some advantages to preparing the restorations in a single appointment. these play a role in shortening the treatment period, renewing it on the same day if necessary, eliminating the need for a temporary restoration, and preventing postoperative sensitivity. (Van Noort, 2012) Today, with the spread and development of this technology, dentists can now easily use many CAD/CAM systems in their clinics (Table-2).

Table 2 CAD/CAM Systems Used in Chairside in Dentistry

System Name	Open / No Access	Software Stability	Production speed	Auto Design Feature	Configuration Properties	Design equipment	Cost
CEREC MC (Dentsply Sirona, USA)	STL Output	Very good	Very fast	Very good	SD Card,	Sufficient	High
Glidewell IO (Glidewell Lab, USA)	STL Input / Output	Good	Medium	No	USB, Wireless	Sufficient	Medium
DG Shape (Roland DG, USA)	STL Output	Medium	Medium	Weak	SD Card, USB,	Medium	Medium
ROLAND DWX (3Shape, Denmark)	STL Input / Output	Medium	Slow	Sufficient	SD Card, USB, Wireless	Medium	Medium
Planmeca FIT (E4D Tech, USA)	STL Input / Output	Good	Fast	Sufficient	USB	Very good	Medium
Dental CS Solutions 300 (Carestream, USA)	STL Input / Output	Very good	Very Fast	Weak	USB, Wireless	Sufficient	Low

CAD/CAM systems offer several benefits to manufacturers, including:

1. **Increased Efficiency:** By using CAD/CAM systems, manufacturers can design and manufacture products faster and with greater accuracy than ever before. This can lead to increased productivity and reduced costs.

2. **Improved Quality:** CAD/CAM systems allow manufacturers to test the functionality of a product before it is manufactured, which can help identify and address potential issues before production begins. This can lead to improved product quality and reduced waste.

3. **Greater Flexibility:** CAD/CAM systems allow manufacturers to make changes to a product design or manufacturing process easily. This

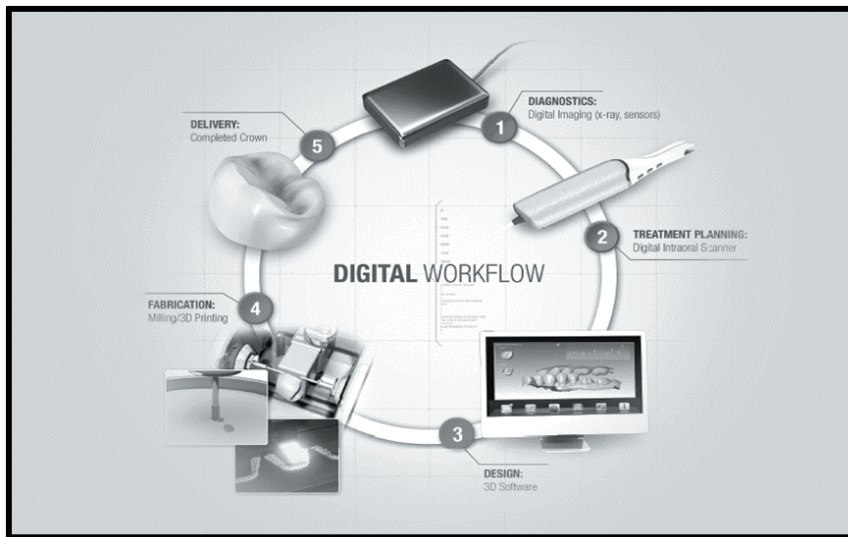
can help manufacturers quickly adapt to changing market conditions or customer needs.

4. **Reduced Costs:** By automating the manufacturing process, CAD/CAM systems can help reduce labor costs and eliminate errors that can lead to wasted materials and time.

5. **Improved Communication:** CAD/CAM systems can help improve communication between different departments within a manufacturing company, as well as with customers and suppliers. This can help reduce misunderstandings and errors and lead to a smoother production process.

In conclusion, CAD/CAM systems have revolutionized the manufacturing industry by allowing manufacturers to design and produce products faster, more accurately, and with greater efficiency than ever before. By integrating CAD and CAM software, manufacturers can create digital models of products, test their functionality, and automate the manufacturing process, leading to increased productivity and reduced costs. As technology continues to advance, CAD/CAM systems will likely become even more sophisticated, allowing manufacturers to produce products that are even more complex and innovative. The Dental Digital workflow is illustrated in Figure 1.

Figure 1 Digital Workflow



3D PRINTERS AND ADDITIVE MANUFACTURING

The growth of dental services and the manufacturing of medical devices are complementary. Using 3D visual models in conjunction with 3D printing technology offers a practical and approachable method. It gives dentists a variety of options, such as easy modeling and previewing,

for the diagnosis and treatment process. A dentist can create personalized designs for a range of product categories using dental 3D printing. The accuracy of products on the market is guaranteed by the effectiveness of digital design, from the planning stages to the production stage. Digital dentistry generally includes a combination of 3D dental printing, computer-aided design and manufacturing (CAD/CAM), oral scanning, design, and 3D printing. 3D applications used for various dental treatments include orthodontic appliances, crown-bridge restorations, implant-supported prostheses, inlay-onlay, and laminate veneer restorations. With CAD and CAM, the various potentials of design and manufacturing have been explored. Besides, most users are diversifying ways to develop dental restorations using 3D printing techniques. Therefore, 3D printing has become a contemporary way of producing medical products quickly and inexpensively.(Cantín, Muñoz, & Olate, 2015) The use of this technique in the dental industry is constantly expanding due to the quick development of advanced medical imaging techniques.(Hassan, Yusoff, & Mardi, 2017) Dental 3D printing techniques include polyjet, stereolithography, selective laser melting, and fuse deposition modeling. Table 3 provides a summary of each technology's principles, structure, benefits, and drawbacks.

Table 3 Modalities and materials for 3D printing.

Techniques	Advantages	Disadvantages	Materials
Selective laser melting	Excellent mechanical qualities and growing	Low effectiveness, poor quality, and high price.	Metal materials. (Torres, 2010)
Polyjet	high efficiency and precision.	Costly and having a short lifespan.	Multiple materials. (Deng, 2017)
Fused deposition modeling	Efficient, green, and affordable.	Surface of the product is easily rough.	Plastics with low melting points. (Malik, 2017)
Stereolithography. Photopolymers and metal. [26]	High processing effect, high precision, and efficiency.	High cost and complex structure.	Metal and photopolymers (Fielding, 2012).

In restorative dentistry, aesthetics is as important as function and hygiene. Therefore, Digital Light Projection (DLP) and Stereolithography (SLA) printers, which can produce epoxy resin-based composite / ceramic hybrid materials and polymerize them with heat and light, have been developed instead of 3D printers.(Jockusch, 2020) The critical factor in both methods is to prepare individual layers of fragments from a photopolymer resin to form the entire restoration, bond them together using an ultraviolet laser, and polymerize them with ultraviolet light. While the main advantages of SLA are the rapid and cost-effective production of a large amount of restoration or model, the most significant improvement in DLP is that the details are important and the material used is optimized

for intraoral conditions.(Anadioti, 2022) Although 3D printers used for restorative dentistry are of different types and features, generally, FDM printers and whitening plates, dental retractors, and isolation sets; Inlay, onlay, veneer restorations, and temporary and permanent crowns can be produced with DLP printers. (Table-4).

Table 4 3D Printers Used in Restorative Dentistry and Their Properties

System Name	Production Technology	Production Material	Area of Use
Sol Ackuretta (Taiwan)	LCD-SLA 3D Printer	Bio-compatible dental resin (Color-Clear)	Permanent onlay restorations, temporary crowns, diagnostic models, surgical guides, night guard plates, splints.
NextDent 5100 (Amman Girsch, Germany)	DLP / SLA / SLS	Bio-compatible dental resin (Color-Clear) and titanium polyamide	Diagnostic models, metal / resin-containing removable and fixed prosthesis infrastructures, temporary crowns and bridges, night protective plates, and implant-mounted couplings.
D100 (Rapidshape, Germany)	DLP	Bio-compatible dental resin (Color-Clear)	Wax-up models, diagnostic models, night guard and surgical guide plates, removable prosthetic skeletons, and temporary crowns.
VarseoSmile Crown + (Bego, Germany)	DLP	Biocompatible ceramic based resin	Surgical guides, night guard plates, permanent onlay restorations, temporary crowns, diagnostic models.
3Demax (DMG Mori, Japan)	DLP	Bio-compatible dental resin (Color-Clear)	Surgical guide plates, night guard plates, temporary crowns, diagnostic models, splints, and impression trays.
Objet 30 Denta Prime (Stratasys, Israel)	DLP	Bio-compatible dental resin (Color-Clear)	Diagnostic models, surgical guides, night guard plates, castable removable prosthetic skeletons, and temporary crowns.
Pro 95 S (Sprintray, USA)	DLP	Biocompatible ceramic based resin	Diagnostic models, night guard and surgical guide plates, removable prosthetic skeletons, temporary crowns and bridges.
Form 3 / 3B (Formlabs, USA)	SLA	Biocompatible ceramic based resin	Permanent onlay restorations, temporary crowns, diagnostic models, surgical guides, night guard plates, splints.
Envision One (Etec, Germany)	CDLM	Bio-compatible dental resin / elastomers	Diagnostic models, temporary crowns and bridges, night guard plates, and surgical guide plates.
Max Pro 4K (Asiga, Australia)	DLP	Bio-compatible dental resin (Color-Clear)	Orthodontic models and brackets, temporary crowns and bridges, clear aligners (surgical / night guard) and splints

DIGITAL SMILE DESIGN

Considering the many treatment options and high aesthetic expectations, a multidisciplinary study is often required to determine the most appropriate treatment course. (Espíndola-Castro, 2019) In traditional treatments, models of patients can be obtained, wax (wax-up) models and

silicone keys prepared, and used in the clinic for this purpose.(An H, 2022) These methods are time-consuming, and it is not always easy to achieve the desired result. Popular applications in dentistry are increasing day by day as a result of our changing perception of time and the formation of high expectations in a short period of time. The use of “Digital Smile Design” (DSD) programs in many cases helps dentists to overcome the previous limitations.(Thomas, 2022) DSD is the digital preparation of the patient’s smile aesthetics, taking into account the condition of the teeth and soft tissues, and presenting the possible result to the dentist and patient by visualizing it. The aim of this method, regardless of the difficulty of the cases, is to guide dentists by both meeting the expectations of the patients and revealing the limitations of the case.(Gürel, 2021) Many different systems and programs produced for this purpose have been made available to dentists (Table 5).

Table 5 Programs Used for Digital Smile Design and Their Features

PROGRAM	COMPANY	FEATURES
Coachman App	Digital Smile Design, Spain	The Coachman App, an improved version of Keynote’s digital smile design, requires three different dental photos. Photographs of the entire face and just the teeth are taken, the first with a complete smile and the second with the teeth at rest. Third, the occlusal angle is used to photograph the entire maxillary arch. The Keynote presentation now includes 45-degree side profile views and videos. Because smile designs are created by hand, they are both time-consuming and subject to subjective evaluation.
Romexis Smile Design	Planmeca Oy, Finland	The program does not need additional support programs to run on Windows or MacOS. First, when the patient naturally smiles, full-face photographs are taken from the anterior region. The software then generates a tooth image with aspect ratios that are determined automatically. It can also identify the colors of existing teeth and detect color and tone using its software, which includes VITA Classic and VITA 3D-Master tooth colors (Vita Scale) in its library.
Smilecloud	SM Biometrics, USA	A cloud-based platform, Smile Cloud allows users to store patients’ medical data, personal data, photos, videos, intraoral scan images, radiographs (OPG and periapical), and computed tomography (B-CT) results. After the photos are uploaded to the system, the algorithm in the software finds the relevant teeth and aligns them automatically. The dentist can change this design if he/she wishes. It can also output in formats (stl, obj) suitable for CAD/CAM and 3D printers.
Smile Designer App / Pro	Neuralp Software Inc, Turkey	Smile Design App, an online digital smile design software, employs the “Smile Design Algorithm,” which is easily and quickly coded. This addition, which includes not only features of the face, mouth, and teeth, but also compositions like “character traits of the patient,” is included in the record. The picture design for all CAD/CAM systems or the design for 3D printers can be output from this software.
3Shape Smile Design	3Shape Company, Denmark	Based on a 2D image taken directly from the patient, 3Shape Smile Design creates a 3D smile design. The 2D image from the dental photograph and the 3D digital scan image from the scanner are combined in the system using the Real View engine. The dentist can create a mock-up model of the relevant teeth before the restoration is completed.
Cerec SW	Dentsply Sirona, USA	According to reports, Cerec SW software uses artificial intelligence to control a variety of operations and algorithms. Software requires a full-face image, allowing for multiple preparations and a limited amount of compatibility with sharper models. It was stated that the image needed to include 16 key points after the file was uploaded to the program. The 2D image is then converted to 3D using various calibrations that the software performs using these points. During the CAD design process, the toolbar’s Cerec Smile Design button can be selected.

Smile Creator	Exocad GmbH, Germany	Existing patient photos or webcam photos are automatically transformed into 3D objects when Smile Creator is integrated into the dental practice's CAD platform, and these 3D objects are then synchronized with 3D scans of the patient's teeth.
Visagi Smile:	Web Motion Co. Turkey	The founder of the Turkish Academy of Aesthetic Dentistry and the previous president of the European Academy of Aesthetic Dentistry both support this program. Galip Gürel was the person who created it. The character and habits of the patient are determined using the idea of "visajism" in another web-based smile design program, and a customized image is created.

DIGITAL COLOR SELECTION

Choosing the right color in dentistry can be challenging due to the subjective nature of natural tooth color and its complex optical properties. To address this issue, the "Munsell Color System" was developed to define tooth color using three values: tone, brightness, and purity (chroma), which are categorized accordingly. However, since tooth color is usually determined by comparing it to color scales prepared using this system, decisions made are often subjective. Additionally, since these color scales do not have numerical values, it is difficult to make a qualitative color measurement. (Chu, 2017)

Fortunately, with the help of advancing technology, colorimeters and spectrophotometers have been developed, which can convert the three basic categories of the Munsell Color System into subcategories with numerical values, leading to more predictable results. These digital color measurement systems also create a color map by determining the distribution of the measured color on the tooth. This map helps dentists and technicians restore tooth tissue that is not uniformly colored (heterogeneous). The numerical values obtained through digital color measurement are based on computer analysis of data received from the device. These devices detect color by measuring the amount of light emitted by the probe, the intensity of light reflected by the device, and the amount of gray shadow detected. (Chang, 2012)

Digital color detection devices offer significant advantages over traditional methods. When determining tooth color with traditional methods, subjective factors such as the conditions of the environment where the measurement is taken, the position and condition of the tooth, and the application parameters of the dentist can affect the final decision. (He, 2020) In contrast, digital color detection devices provide objective data that can be stored as a safe resource for dentists and patients in applications where pre- and post-recordings are essential, such as in whitening treatments. This feature can significantly increase the accuracy and reliability of the color determination process. (Huang, 2022)

CONCLUSION

The digitalization of techniques and methods used in dentistry has significantly improved the quality of treatments while saving time and

cost for dentists. In challenging and subjective situations such as color detection and differentiation of carious tissue, digital equipment offers convenience and guidance to dentists for accurate diagnosis and treatment. Additionally, the increasing use of CAD/CAM and 3D printers in dentistry has revolutionized the production of dental restorations, allowing for faster, easier, and more compatible results.

These technological advancements not only provide convenience to dentists but also offer patients a sense of comfort and complete confidence in their treatment. It is essential for dentists to choose equipment suitable for their working style and clinical conditions and to use them effectively to achieve absolute success.

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CHAPTER 6

AUDITORY-VERBAL THERAPY

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1. Introduction

Hearing loss is defined as the problem experienced in perceiving acoustic sound signals due to a defect in any part of the auditory pathways (Avcioğlu, 2008). Since hearing loss is a condition that affects the steps in speech and language development, early diagnosis and the use of early intervention methods have an extremely critical place in the acquisition of the expected language skills related to the chronological age of the child.

Hearing losses that occur at an early age affect children's auditory perception (Sininger et al., 2010), speech and language skills (Blamey et al. 2001; Ansari, 2004; Carey-Sargeant and Brown; 2005), verbal communication (Vaccari and Marschark, 1997; Lederberg et al. Everhart, 2000) negatively affect their cognitive skills and academic progress (Marscharch et al., 2007). Studies have shown that the negative effects of hearing loss are reduced by early diagnosis and the use of early intervention methods (Yoshinaga-Itano et al., 1998; Moeller, 2000; Kennedy et al., 2006).

Thanks to the rapidly developing hearing aids and cochlear implant technologies, the level of expectation regarding the listening and speaking language skills of children with hearing loss and their performance in academic and social life has increased (Moeller, 2000; Svirsky et al., 2000; Yoshinaga-Itano et al., 1998). Children between the ages of 0-3.5, who have been shown as the critical period thanks to early diagnosis and intervention, who have had hearing aids or cochlear implants; they can have the chance to develop at a similar level to the language and speech development of their normally-hearing peers (Lim & Simser, 2005).

Thanks to the newborn hearing screening programs being implemented around the world, including our country, it has become easier for children with hearing loss to access oral language with early diagnosis of hearing loss and early instrumentation in accordance with hearing loss (Moeller, 2000; Svirsky et al., 2000; Yoshinaga-Itano). et al., 1998). Thanks to the developments in education and technology, the increase in access to oral language plays a role in the preference of verbal education methods (Warner-Czyz et al., 2009).

Auditory-verbal therapy, which is one of the verbal education methods, is a communication and early intervention method that aims to teach the child's ability to use their hearing in the normal course of life by incorporating spoken language into daily activities (Estabrooks et al., 2016; Estabrook et al., 2020). The basic principles of auditory-verbal therapy were established by the pioneers of this therapy method, Daniel Ling, Doreen Pollack and Helen Beebe. The main purpose of this method is to raise the receptive and expressive language skills of the child with

hearing loss to the level of their peers (Beebe, 1933; Ling, 1933; Pollack, 1933). Since language development occurs with the active and effective use of the sense of hearing, the child is intensely exposed to hearing stimulation in therapies. It is aimed to provide speech and language development in children by focusing on listening (Brennan-Jones et al., 2014; Dornan, 1999; Eriks-Brophy, 2004). In order to achieve this goal, it is very important for experts and parents to cooperate and be in harmony.

2. Basic Principles of Auditory-Verbal Therapy

Auditory-verbal therapy has 10 basic principles developed by Pollack (1970) and revised by The AG Bell Academy for Listening and Spoken Language (2006) (Estabrooks, 1994; Estabrooks, 2007; Diller, 2007):

Principal 1: The diagnosis of hearing loss in infants and young children should be made as soon as possible, and appropriate audiological intervention and auditory-verbal therapy should be initiated.

Delayed diagnosis of hearing loss causes negative effects on the child's social, psychological, cognitive and communication skills. With the Newborn Hearing Screening Program in our country, babies are diagnosed before they are 3 months old, and when they are 6 months old, they are included in rehabilitation programs suitable for loss. In this way, it is ensured that the child with hearing loss does not fall behind the language and speech development level of his peers and uses only spoken language in communication (Brennan-Jones et al., 2014).

Principal 2: Appropriate hearing aid or cochlear implant should be applied in order to get the maximum benefit from the auditory stimulus.

After the application of a hearing aid and/or cochlear implant suitable for the type and degree of hearing loss, intense exposure of the child to auditory stimuli in the 0-3.5 age range, which is specified as the critical period, will ensure that the child does not fall behind in terms of language and speech development (Sharma et al., 2005; Sharma and Glick, 2016; Yoshinago-Itano, 2003).

Principal 3: Parents should be guided to use hearing as a primary sense method for the development of children's speech and language skills.

The acquisition of language and speaking skills and the development of social, psychological, cognitive and communication skills depend on the processing of auditory information and the development of listening skills. If parents support their children in developing their listening skills, children will be willing to communicate even in noisy environments (Hepper and Shahidullah 1994; Lieu, 2004; Olusanya et al., 2004; Pimperton and Kenndy, 2012; Yoshinaga et al., 1998).

Principal 4: Parents should be guided that their regular and active participation in individualized auditory-verbal therapy for their child plays a facilitating and important role in the development of the child's speech and language skills.

Auditory-verbal therapy sessions should be carried out in collaboration with parents-therapists, as auditory-verbal therapy specialists guide parents about the methods to be applied during the process of gaining language and speech skills of their children. The therapist transfers the strategies that can improve the child's hearing, speech, language and communication outside the therapy environment to the parent, and the parent ensures that these strategies are integrated into the child's daily activities (Estabrooks et al., 2016; Estabrooks et al., 2020).

Principal 5: Parents should be guided to create environments that are suitable for the development of speech and language skills and that support listening during the daily activities of their children.

The presence of a variable background noise in the environment where children perform their daily activities, unlike the therapy environment, may cause difficulties for the child with hearing loss to participate in the communication network in the listening environment and to develop their communication skills. Due to the intense need for auditory stimulus in the process of acquiring language and speaking skills, the child's listening skills are first developed in the therapies, and then various applications are made to develop this listening skill gradually in noisy environments. In this way, the child can analyze and communicate auditory stimuli even in noisy environments (Estabrooks et al., 2016; Estabrooks et al., 2020).

Principal 6: Parents should be guided to integrate listening and spoken language into all areas of their children's lives.

In order to create an individualized auditory-verbal therapy program, the daily routines of the family should be transferred to the therapist. In therapies, the methods applied while the child gains listening skills and the activities that the family can transfer to their daily routines are shown to the family by the therapist, so that the parent and child are evaluated not only for the therapy session but also for every moment of the day for listening, language and speech development. As these activities are repeated both in therapy and in the home environment, the child's listening skills improve, families who see improvement understand the benefit of therapy and are motivated to do more activities (Leffel & Suskind, 2013).

Principal 7: Parents should be guided to follow their children's use of hearing, speech, language, cognitive and communication skills in the natural developmental process.

Appropriate short- and long-term goals for the effectiveness of therapy should be set by the therapist and parent. The therapist should guide parents to close the developmental gap between the child's hearing age and chronological age as quickly as possible by using appropriate strategies (Estabrooks et al., 2016; Estabrooks et al., 2020).

Principal 8: Parents should be guided to support their children in following their own spoken language through listening.

As the child learns to listen using a hearing aid and/or cochlear implant; develops language and communication skills, expands the vocabulary, starts to form sentences with rules, and learns to use the internal and external feedback mechanism used during speaking, thus starting to speak fluently (Estabrooks et al., 2016; Estabrooks et al., 2020).

Principal 9: Auditory-verbal therapy sessions should be individualized and developed, and appropriate planning should be made for the child and family in order to monitor the development.

While creating the therapy program, the therapist should observe and evaluate the development of the child and family; should consider the needs of the child and family and the problems that develop in addition to the child's hearing loss (Estabrooks et al., 2016; Estabrooks et al., 2020).

Principal 10: From an early age, it should be ensured that the child receives education in normal classrooms with his/her hearing peers, using appropriate support services.

The therapist helps the parents acquire the child's communicative skills and should provide guidance on starting the education. In order for the child to feel safe, the entire auditory-verbal therapy team should act in cooperation and harmony from the moment they start school education (Langeris & Vermulen, 2015; Yoshinago-Itano, 2003).

The 10 items above are the basic principles of Auditory-Verbal Therapy and aim to maximize the benefit from therapy.

3. Components of Auditory-Verbal Therapy

3.1 Auditory-Verbal Therapy Team

Auditory-verbal therapy; It is a teamwork that requires a multidisciplinary approach, based on the child and family. In the auditory-verbal approach, each session is planned individually; It is carried out with the joint participation of the family and the therapist.

While child, family, audiologist, ENT specialist, Language and Speech Therapist and auditory-verbal therapist are the primary team members in the auditory-verbal therapy team, the team also includes a

nursery/kindergarten teacher, special educator, pediatrician, psychologist, classroom teacher and social worker. can be found (Estabrooks, 2007).

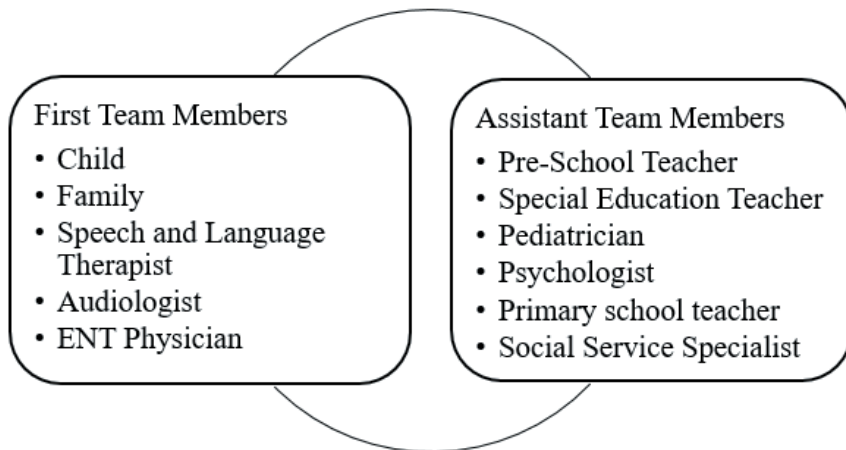


Figure 1 Team Members in Auditory-Verbal Therapy (Estabrooks, 2007)

3.2 The Importance of Family and Family in Auditory-Verbal Therapy

In the auditory-verbal therapy method, the family is one of the cornerstones of the therapy team. The fact that their children have hearing loss can negatively affect some functions of the family and cause various problems in controlling their behavior towards their children (Şahlı et al., 2011). It is very important for the family to benefit from psychological and social support services in order to build healthy relationships with their children and their environment (Calderon, 2000; Watkin et al., 2007, Holzinger et al., 2011; Şahlı et al., 2011). In the auditory-verbal therapy process, families; They have responsibilities such as making joint planning with the therapist and informing the therapist, including more auditory stimuli in their daily activities, interpreting the child's communication skills correctly, and displaying a supportive and motivating approach to the child (Estabrooks, 1994; Estabrooks, 2007; Diller, 2007). Every family may not show equal desire and effort to participate in this process, but it should be noted that the effectiveness of the child-family relationship in the auditory-verbal therapy process is much more effective than the effectiveness of the child-therapist relationship (Estabrooks, 1994; Watkin et al., 2007; Brennan-Jones et al. , 2014).

3.3 Auditory-Verbal Therapy Sessions

Auditory-verbal therapy; consists of individualized sessions in which the therapist, family and child participate. Sessions lasting approximately

1-1.5 hours are usually held once a week; Increasing the number of sessions can show advantages or disadvantages according to various variables (Estabrooks, 2007).

Auditory-verbal therapy sessions are planned considering various features such as the child's chronological and hearing ages, intelligence level, the development of auditory perception, and the socio-cultural status of the family, and are aimed at 5 developmental areas of the child, namely hearing, speech, language, cognition and communication (Estabrooks, 2007). Each session includes the steps of setting goals, receiving feedback from the family, demonstrating techniques and strategies, periodic evaluation, interpreting the process and making suggestions.

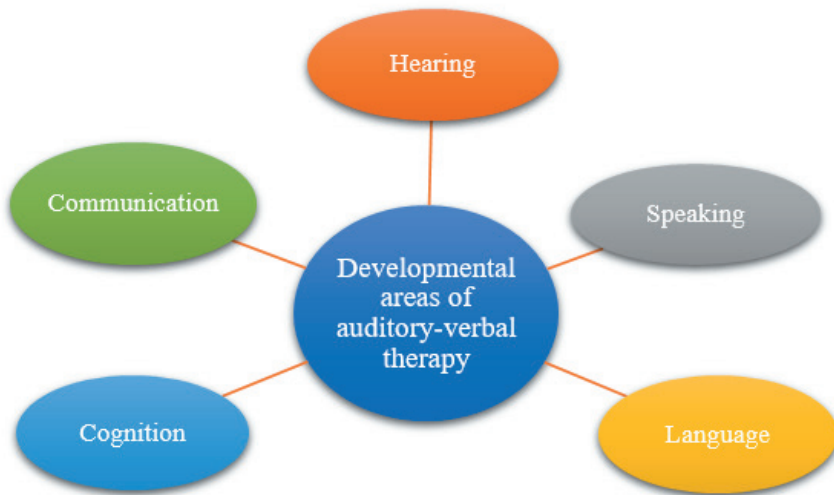


Figure 2 Developmental areas of auditory-verbal therapy (Estabrooks, 2007)

Since the auditory-verbal therapy technique is based on listening rather than visual stimulus, it is extremely important that therapy sessions are carried out in acoustically appropriate environments. During therapy; The listening environment can be improved by methods such as the therapist sitting close to the child on the side of the hearing ear, being in a position where the child's hearing aid and/or the microphone of the cochlear implant used by the child can hear the sound comfortably, and reducing the background noise to the lowest possible level (Estabrooks, 1994; Estabrooks, 2007). ; Diller, 2007).

Incorporating the practices and activities learned by the family by observing the therapist during the session to the child's daily activities plays an important role in increasing the efficiency of the therapies and in the development of the child's listening skills.

4. Techniques Used in Auditory-Verbal Therapy

4.1 Hand Cue Technique

The ‘Listen!’ sign made by showing the ear with the hand is called the Hand Cue technique. With this sign, it is aimed to direct the child’s attention to the sound and to develop the skill of listening carefully. While applying this technique, the therapist’s mouth and lips should be out of the child’s field of vision in order to ensure that the child focuses on the acoustic stimulus rather than the visual stimulus. It is stated that this technique is a very useful technique for children who seek visual stimuli in speech, and it is used less and less as their listening skills develop (Hanáková, 2014; Simser, 2014).

4.2 Acoustic Emphasis

The acoustic accentuation technique is the accentuation of a specified word, phrase or phrase in order to differentiate it from the rest of the message. Acoustic accentuation technique is frequently used in the early stages of listening skill and is also called ‘mother’ or ‘parent talk’. Like the Hand Cue technique, this technique is used less and less as listening skills develop (Simser, 2014).

4.3 Auditory Feedback

Auditory feedback is a necessary factor in language and speech development. When children speak or imitate spoken words, they compare the sound they produce with others. In this auditory feedback, asking children to imitate the sounds they hear helps confirm the accuracy of what the child hears (Brainard & Doupe, 2000; Simser, 2014).

4.4 Pausing and Waiting

The pausing and waiting technique encourages children with hearing loss to focus on listening rather than waiting for the speaker to repeat, as auditory stimuli take longer to process than their normally-hearing peers. This technique helps to develop the child’s ability to make sense of the message that he cannot fully understand and is one of the useful techniques, especially at the beginning of the language acquisition process (Estabrooks, 2006, Simser, 2014).

4.5 Showing the Object After Giving an Audible Stimulus

In order to increase the level of auditory perception rather than visual perception, the toy or object to be used in therapy is first given the sound (for example, whistling before showing the car, waving before showing the toy dog), then the relevant material is shown to the child (Estabrooks et al., 2016; Estabrooks et al., 2020).

4.6 Leaning Towards and Approaching the Child

When communicating with the child, it is shown by body language that there is an expectation of an answer to the question by leaning slightly towards the child when the child is expected to respond (Estabrooks et al., 2016; Estabrooks et al., 2020).

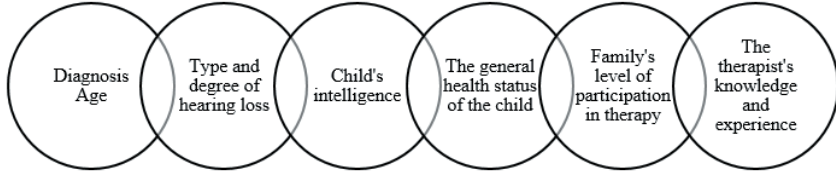


Figure 3 Factors affecting the success of auditory-verbal therapy (Estabrooks, 2007)

In the auditory-verbal therapy process, it should not be forgotten that each child's listening and communication development is different from each other, and each child's learning style is different. The success of these techniques; Factors such as the age at diagnosis, the type and degree of hearing loss, the intelligence and general health of the child, the level of participation of the family in therapy, and the knowledge and experience of the therapist are directly related (Estabrooks, 1994; Estabrooks, 2007).

5. Various Studies on Auditory-Verbal Therapy

Durieux-Smith (1998), in his study examining 65 adolescents over the age of 14 who have been educated with auditory-verbal therapy since the pre-school period, revealed that auditory-verbal therapy was effective in school and community life, and the adolescents participating in the study achieved high scores in communication, self-perception and academic skills came to the conclusion.

Goldberg and Flexer (2001) found that 72.7% of children participate in the hearing and speaking world, and 95% of them continue to secondary education, in their study in which they examined 157 children with severe and profound hearing loss who received auditory-verbal therapy for at least 3 years. have reported that.

Rhoades and McCafferey (2002) reported in their study, in which they observed 40 children with hearing loss who received auditory-verbal therapy for 4 years, that they reached a significant difference in terms of language development after therapy, that at the end of the process, the gap between the children's chronological ages and language ages closed and they approached the results of children with normal hearing.

Dornan et al. (2009), in their study comparing the speech and language development of 25 hearing-impaired children aged 2-6 years and receiving

auditory-verbal therapy, with their normal-hearing peers reported that their scores increased statistically significantly and reached almost the same level as their peers with normal hearing. Şahlı and Belgin (2011) reported that the auditory perception development of 15 children with hearing loss who received auditory-verbal therapy was evaluated before and after the cochlear implant operation (1-3-6-12. months), and that auditory perception development reached the highest level in the 12th month.

Jackson and Schatschneider (2014) evaluated 24 children with hearing loss who received auditory-verbal therapy with a preschool language scale at 6-month intervals and reported that the language scores of children with hearing loss were close to the language scores of their peers with normal hearing. Monshizadeh et al. (2018) compared the social skills of 30 children with cochlear implants aged 7-8 who participated in auditory-verbal therapy sessions before and after implantation with those of their peers with normal hearing. They observed that the social skills of children with hearing loss who participated in the study improved positively.

Minami et al. (2021), as a result of the study in which they included children who were 5-6 years old at the time they carried out the study and who started auditory-verbal therapy sessions before the age of 1; with the effect of auditory-verbal therapy in the early period, the use of hearing aids and cochlear implants, improvements in the level of hearing perception of children with hearing loss have been observed. They have shown that cochlear implant application is more effective than hearing aid application in providing the development of listening and language skills in children with hearing loss whose hearing thresholds are more than 90 dB HL and whose thresholds are more than 40 dB HL with devices.

This and similar studies reveal that the use of auditory-verbal therapy is extremely effective for children with hearing loss to catch up with the language and speech levels of their normal hearing peers, to keep their academic performance high and to avoid problems in their participation in social life.

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CHAPTER 7

AMBULANCE ACCIDENTS BETWEEN 2016-2021 AND THEIR INVESTIGATION IN TERMS OF OCCUPATIONAL HEALTH AND SAFETY¹

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Ambulance is defined as a vehicle used to treat and transport emergency patients in a hospital. The term “ambulance” is derived from the Latin word “ambulare” meaning “to walk or move”. With the population growth in India, medical services in general and Emergency Medical Services in particular have lagged behind. The concept of ambulance was originally designed by the French military surgeon Dominique Jean Larrey during the Battle of the Tower (a war between France and Prussia) when he used chariots pulled by two or four-wheeled horses for first aid, with the aim of comforting and helping the wounded. It was used in everything from evacuating soldiers from the battlefield to quickly transporting them to nearby military casualties. The concept was approved by the Committee of Public Safety in 1796 during the Italian campaigns. With the advent of the automobile in the 19th century, the first motorized ambulance was introduced in 1906. Gas powered vehicles were used to transport a number of patients during the First World War. Gradually, motor vehicles and then ambulances were created (Kurian, 2020) (Figure 1).

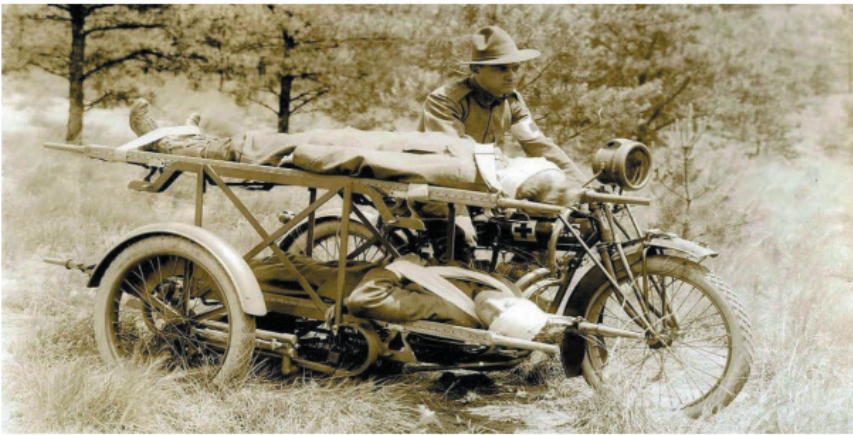


Figure 1. *Ambulance in history (Aksu, 2020)*

Ambulance services in many countries go through three successive stages of development and transformation. The importance of ambulance service was first understood on the battlefields, and then ambulances were partially experienced in the civil sector in various disaster situations. In the third stage, ambulance service was introduced to the country’s health system under the name of “ambulance service”. Although ambulance services show some structural differences in each country, they generally appear as structures for the same purpose. This historic three-stage transition of the ambulance service is also valid for Turkey. As part of the second phase of development, quite broad powers have been given to various administrative and institutional bodies in emergencies such as natural disasters. Within this jurisdiction, the question of how and by what

vehicle the injured will be transported to medical facilities has been one of the most prominent questions. However, ambulance service emerges as a broad system that includes various fields such as telecommunications, media, education, technical equipment, qualified health personnel and advertising. The importance of using ambulances to transport the sick and wounded was also of great importance in the early days of the Republic, thanks to the experience gained on the battlefields. It was known that the Ottoman Empire provided transportation facilities for patients by motor. These engines were used as ambulances on many fronts during World War I. In the 1980s in Turkey, state hospitals and some private hospitals used various means of transportation to take patients from home to the hospital. However, it is seen that this activity is not an ambulance service in the current sense, but a patient transport service that can be defined as a social service and is considered as a vehicle open to the use of private hospitals. The use of disaster ambulances, which is the second stage in the development of ambulance services, was developed after a transition period, with the compulsion of the Civil Defense Head of the Ministry of Interior instead of the Red Crescent. The Head of Civil Defense has also published training guides on ambulance services and organized various studies and trainings for disaster response. The book “First Aid and Ambulance Services”, which was first published in 1968 and published three times with various updates until the 077 Hızır emergency service was established, is the first Turkish guide on ambulance service in its field. In the book published by the Ministry of Civil Defense, ambulance services were primarily carried out within the framework of a military system (Sofuoglu, 2018).

1. Types of Ambulances Used

Causes such as disaster, great damage, destruction, ecological deterioration, accidents that cause loss of human life, inadequate health and health services make it necessary to intervene. In general, all events with significant destructive effects pose a great threat to human life. Of course, the response and recovery phase is needed under acutely challenging conditions. Limitation of treatment capacity (transport vehicles, manpower and hospital capacity), with uncertain information about the number, damaged roads or transport infrastructure poses vital risks for injured people. On top of that, emergency service is essential and requires an ambulance to quickly initiate the necessary logistical aid operations, manage and control effective aid flows, and meet the immediate needs of the affected people. As a result, there is a need for ground support vehicles that offer instant solutions to problems as an indispensable support. The issues of determining the location and dispatching of ambulances as emergency medical aid are discussed (Tikani and Setak, 2020). Ambulances in Turkey

are divided into three as ground, water and air ambulances. These are also separated within themselves (URL-1, 2022) :

1. Ground Ambulances

- Emergency ambulance
- Patient transport ambulance
- 4 stretcher intensive care ambulance
- Obese ambulance
- Newborn ambulance
- Motorized ambulance
- Specially equipped snow ambulance

2. Water Ambulances

- Çanakkale (Imbros),
- Balıkesir (Marmara Island),
- There are six sea ambulance boats available in Istanbul (Büyükdere, Büyükdere).

3. Air Ambulances

- **Aircraft Ambulance:** Ambulance planes that have been used since 2010;

One with 4 stretchers,

One with 2 stretchers,

One with single stretcher

These three ambulances serves.

- **Helicopter Ambulance:** Air Ambulance service was started with two Helicopter Ambulances, which started service on October 28, 2008. It was expanded in March 2009 by increasing its number. At the moment; Twelve Helicopter Ambulances provide service, one each in Ankara, Istanbul, Izmir, Adana, Antalya, Diyarbakir, Erzurum, Kayseri, Konya, Samsun, Trabzon and Van.

The most frequently transported patient group by ambulance helicopters is cardiac patients. This is followed by brain and nervous system patients, trauma, respiratory diseases, traffic accidents, gastrointestinal system diseases, newborn cases, infectious diseases and other emergencies.

2. Interior Equipment and Technical Team of Ambulance

Considering the interior equipment of ambulance vehicles, it is expected to comply with the legislation. In this direction, the legislation suitable for ambulance interior equipment is as follows:

ARTICLE 5

(1) Ambulances are classified as land, air and sea ambulances according to the mode of transportation. Land ambulances are also classified as emergency ambulance, patient transport ambulance, intensive care ambulance and specially equipped ambulances according to their intended use.

<p>A) GROUND AMBULANCES:</p>	<p>1) Emergency ambulance: It is a land vehicle with the technical and medical equipment listed in Annex-1 and Annex-2, and the team that can provide the necessary emergency medical attention to the sick and injured in all kinds of emergency situations, at the scene and in the ambulance.</p> <p>2) Patient transport ambulance: It is a land vehicle with at least one health personnel and technical and medical equipment specified in Annex-1 and Annex-2, used for the transportation of patients or injured people who do not require emergency medical attention.</p> <p>3) Intensive care ambulance: It is a land vehicle with technical and medical equipment included in Annex-1 and Annex-2 of the Regulation, designed for advanced monitoring and treatment of patients during transport.</p> <p>4) Specially equipped ambulances: These are vehicles that are specially designed and equipped with personnel and equipment according to the geographical characteristics of the area where they work, and the age, physical and medical conditions of the sick or injured people. Ambulance conformity certificate of specially equipped ambulances is registered by the authorized traffic units after it is issued by the directorate in accordance with Annex-6, with the approval of the General Directorate. Ambulances to be used for the transport of newborn patients; In addition to providing the medical and technical equipment of the emergency ambulance, it must have a transport incubator with ventilator. Medical equipment and materials to be used in adult patients are not required in these ambulances. Registration of specially equipped ambulances such as all-terrain snow crawler, multi-patient, obese patient, hovercraft, land, sea and snowmobile, pedal or motorized bicycle and ATV; It is done with an ambulance conformity certificate to be issued by the directorate in accordance with Annex-6, by taking the approval of the General Directorate in terms of its technical and medical characteristics.</p>
<p>B) AIR AMBULANCES:</p>	<p>They are airplanes and helicopters that have received work and flight permission from the national civil aviation authorized unit to be used for patient transport or emergency medical intervention and have the medical equipment specified in Annex-3.</p>
<p>C) WATER AMBULANCES:</p>	<p>They are sea vehicles with the medical equipment specified in Annex-3, which have received a work permit from the Ministry of Transport, Maritime Affairs and Communications to be used for patient transport or emergency medical intervention.</p>

(2) Patient transport vehicles operate under public institutions and organizations and private health institutions. After obtaining the vehicle modification certificate from the Turkish Standards Institute and obtaining

the patient transport vehicle conformity certificate from the directorate in accordance with Annex-6, it is registered by the authorized traffic units. At least one health personnel is present during transportation in these vehicles. Patient transport vehicles have at least the following equipment:

- Communication devices (radio or telephone),
- Phosphorous writings and signs indicating the intended use of the vehicle,
- One blood pressure monitor, one portable oxygen unit, automatic external defibrillator and one basic medical equipment bag.
- Vehicle tracking and navigation systems (URL-2, 2022) (Figure 2).



Figure 2. *Interior Equipment of Ambulance (Aksu, 2020)*

3. Occupational Health and Safety Risks That Ambulance Personnel May Encounter

Occupational health and safety legislation is an important part of the process of managing organizations and companies. However, there are also criticisms that occupational health and safety regulations may limit innovation and industrial development impulses. This has led to proposals to repeal regulations to reduce the regulatory burden whenever possible. This study aims to investigate the difficulties that organizations face in their efforts to comply with occupational health and safety legislation and to manage the process effectively. A systematic review of published studies examining the relationship between occupational health and safety (OHS) management and compliance with legislation, regulation and rules has been made. International bibliographic databases and scientific search engines were mainly used to search for related publications. Quotations from other authors were also examined. This review provides information on how compliance and non-compliance affect the day-to-day health and safety management of companies. The review highlights and discusses

both successful regulatory strategies and the key challenges, weaknesses, limitations and challenges companies face in adopting and adapting to those regulations. This study concludes that compliance management has become a complex task in companies, especially in small and medium-sized enterprises. The management of occupational health and safety systems should not only be based on prescriptive principles and the detection of nonconformities, but also a scraping should be provided by taking into account possible situations (Salguero-Caparrós, 2020).

Prehospital paramedics are the team that goes to the scene and initiates medical care in the event of an illness or disaster that disrupts daily life. Emergency medical technicians, paramedics, nurses, paramedics drivers are included in this group. These staff often make quick decisions, act quickly, and are preoccupied with providing medical care to critically ill patients in unsuitable patient conditions, on the verge of criticism, curiosity, or tension in their environment. Health workers who provide emergency pre-hospitalization care are more affected by this situation than other health workers because they start emergency medical care. Ambulance workers, who spend most of their time in the open air by providing emergency health services, are in a more disadvantaged group compared to all health workers in terms of occupational health and safety. Although rapid and effective medical care is provided in an emergency, environmental conditions, stress of employees and those around them, inadequacies, accidents at the workplace or occupational disease are quite challenging. However, the Occupational Health and Safety Law No. 6331 does not cover emergency and disaster units response activities that may increase the risk, except for the Law No. : 6331). In terms of occupational health and safety, while the comfort, temperature, wind, humidity, noise and lighting conditions cannot be kept constant for these employees in emergencies and disasters, it increases the risk of biological and severe threats to patients and their loved ones. Pre-hospital emergency services abroad are described as a group of “high risk” occupations due to the stressful nature of the job (URL-3, 2022).

4. Ambulance Accidents

While traffic accidents, one of the most important causes of injury and death in the world, pose a serious risk of death for all humanity, it is of greater importance for pre-hospital emergency personnel as a significant part of their working time depends on traffic. Ambulance usage becomes more difficult for personnel working under time pressure when traffic rules are incomplete or unclear. In this respect, it is possible to say that the study groups are superior to other groups. It has been shown that the risk of death in an ambulance car accident performed by emergency health personnel before applying to the hospital in Turkey is 21 /100.000 per year, while

the rate is 9.6/100.000 in other countries. Health personnel working at 112 ambulance stations in Istanbul determined the risk score of Emergency Medical Technician. They found that they had an ambulance accident at least once in the last 2 years (2014-2016). Speed is one of the primary problems at the crossroads. Transfer of ambulance driver to safety and health personnel since 2012, lack of experience and increased workload (increase in visits) is another issue that causes the risk of traffic accidents to increase. It shows that it may be one of the important reasons for the increase in the number of cases due to the 2.9 growth experienced in the emergency health services sector in the 5 years between 2009 and 2013. Going to the shift while resting, using an ambulance according to the traffic rules, not drinking before the shift, not taking distracting drugs, and reducing the workload by increasing the number of stations will be effective in reducing this risk. Although the ambulance stations are in use 24 hours a day, 7 days a week, the lack of personnel responsible for the cleaning of these stations due to the limited time of the user can make the cleaning of the station limited (Yıldırım and Gerdan, 2017).

Among the ambulance/traffic accident studies, Akmut (2019) found that almost half of the participants had a traffic accident. According to the results of Ekşi and others study, when the last 5 years of research were examined, it was concluded that ambulance accidents increased. In the study conducted by Gülen and others (2016), it was determined that the majority of the sample group had experienced an ambulance accident at least once (Karagöz and Maya, 2021). Ambulances are no different from other vehicles in traffic, and these vehicles can only be used by gaining superiority on the road with the permission of the driver of an oncoming vehicle. Vehicle drivers are also responsible for all traffic rules while participating in traffic. The law does not give any advantage to the ambulance as it violates the traffic rules. Even ambulance drivers knowing this information can prevent many ambulance accidents. In ambulance accidents, the target should always be zero accidents. The ambulance driver has to accept zero risk in this case. The safety of emergency medical personnel, patient and the environment continues to be a priority during patient transport. When the ambulance arrives for the patient, the safety precautions regarding driving while the ambulance is parked should be restarted. Ambulance accidents are experienced both by acting without paying attention to these rules and by ignoring some issues (Figure 3). These are generally; It is caused by speeding, accidents due to intersections, sleepless and tired driving, maneuvering errors and lane and overtaking errors. It is also another cause of traffic accidents caused by ambulance construction. Although the number of ambulances is increasing day by day in our country, ambulances are still not produced as personal vehicles,

but modifications (without any mechanical modification) are produced for commercial vehicles. The most basic information we know is that the focus has changed with the conversion of manufactured vehicles such as commercial vehicles into ambulances. Again, since ambulance conversion vehicles are not produced for this purpose, there is no additional safety measure in the patient compartment. In this case, of course, it causes accidents. (Lee and Shin, 2018).



Figure 3. *An ambulance accident (URL-4, 2022)*

MATERIAL & METHOD

This study was conducted to evaluate the ambulance accidents in Turkey between the years 2016-2021 and the investigation of their causes. The pre-hospital part of the emergency health services in our country is carried out by 112 emergency health stations affiliated to the provincial ambulance services established in the provinces. General practitioners, ambulance and emergency care technicians, emergency medical technicians and vehicle drivers work at these stations. In some stations, ambulance and emergency care technicians and emergency medical technicians are the drivers of vehicles. After the emergency call is received, the incident is questioned by the command and control center as soon as possible and the nearest and most suitable emergency health station ambulance is directed to the scene via radio or telephone. The team is both guided and followed in terms of instant location information with the satellite tracking system from the digital maps in the center before and after the event. This organizational working system, operating in a seven days and 24h system, the number of cases, the time to reach the case, the

quality of training of the teams and the results of the first response appear as important indicators for making international comparisons (İnci et al., 2016). In order to obtain information about ambulance types, information was provided by using the page of the Ministry of Health. Information on how the interior equipment of the ambulance was formed was taken from the legislation and used. Then, the definition of occupational health and safety was explained, and occupational health and safety was evaluated in terms of information and health personnel. Occupational health and safety risks of ambulance users, who are among the health personnel, which constitute the main part of our study, were evaluated and the risks they experienced were evaluated.

RESULTS

As a result of the internet research, the total ambulance accidents between the years 2016-2021 are given in Figure 4 below.

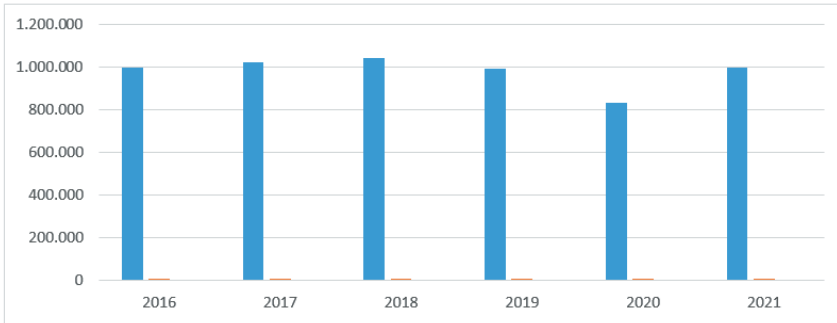


Figure 4. 2016-2021 Total accidents (URL-5, 2022)

As can be seen in Figure 4, the effects of the 2020 pandemic are seen in a positive way, and compared to other years, accidents have decreased as the pandemic empties the streets. It is seen that accidents occurred the most in 2018. When we come to 2021, it is observed that accidents have increased significantly in this period compared to 2020. As a result of the internet research, the types of accidents between 2016-2021 are given in Figure 5 below.

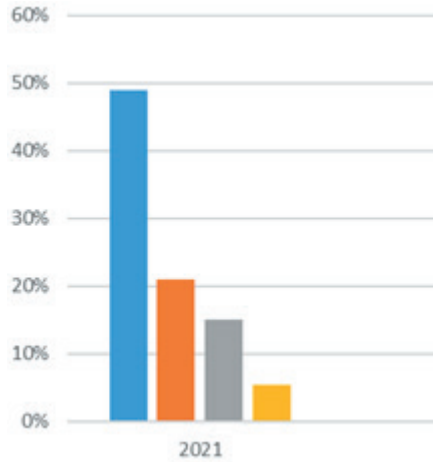


Figure 5. 2021 - Types of accidents (Blue-car, Orange-motorcycle, Grey- Pickup truck, Yellow-ambulance) (URL-5, 2022)

As a result of the internet research, the types of accidents between 2016-2021 are given in Figure 6 below.

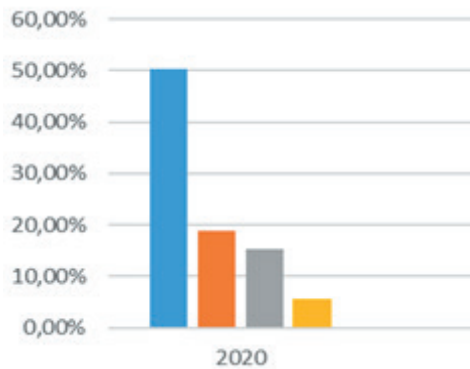


Figure 6. 2020 - Types of accidents (Blue-car, Orange-motorcycle, Grey- Pickup truck, Yellow-ambulance) (URL-5, 2022)

When Figure 5 and 6 are examined, it is observed that ambulance accidents are less than other vehicle accidents in 2020 and 2021. Although it is not included in the majority of the denominator, even the fact that ambulance accidents are in the 5% slice is extremely important in terms of being included in a risk group. As a result of the internet research, the reasons for the accidents between the years 2016-2021 are given in Figure 7 below.

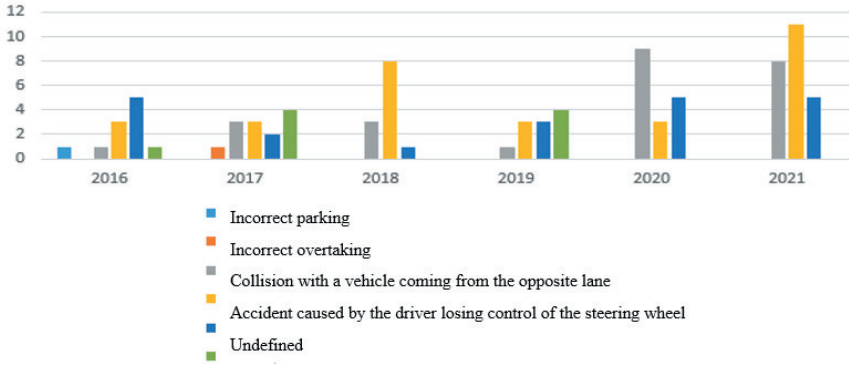


Figure 7. Causes of accidents by years (T.R. Ministry of Health, Health Information Systems Yearbook, 2020)

Looking at Figure 7, when the causes of accidents between the years 2016-2021 are examined, it is determined that the accidents due to incorrect parking show an imbalance between the years and have decreased one by one. It is seen that the accidents caused by improperly passing were not seen at all after they were seen only in 2017. It is seen that the most accidents caused by collisions with those coming from the opposite lane are in 2020, and at the same time, while this rate was very low in previous years, it has increased quite rapidly in recent years. It is seen that there is an imbalance compared to the years in which it has increased in recent years, and it is observed that it is especially observed in 2021 at the most.

As a result of the internet research, the number of dead and injured in accidents between 2016-2021 is given in Figure 8 below.

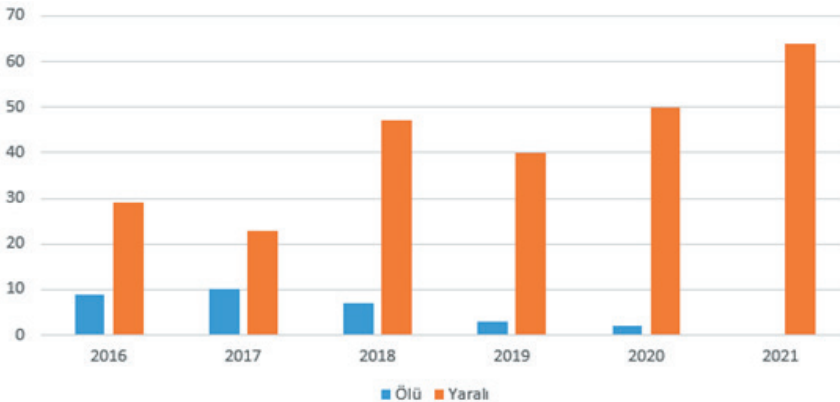


Figure 8. Number of dead and injured in accidents by years (T.R. Ministry of Health, Health Information Systems Yearbook, 2020)

When we look at the rate of change of the dead and injured according to the years, which are discussed in Figure 8, although the number of deaths due to the accident is very low, it has decreased over the years and there is no death toll in 2021. As a result of the internet research, the numerical distribution of ambulance types used between 2016-2021 is given in Figure 9 below.

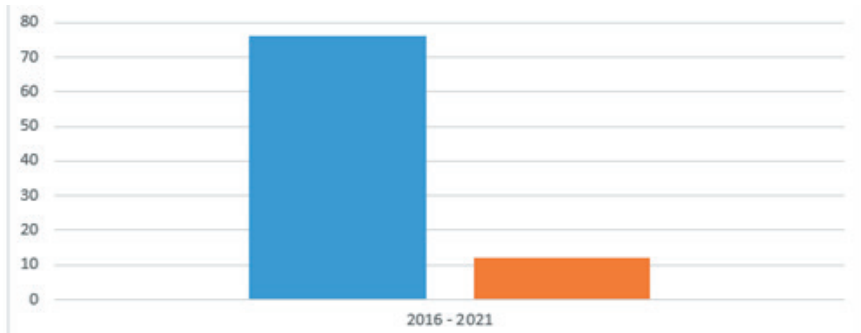


Figure 9. Numerical distribution of ambulance types used (Blue-112, Orange-others) (T.R. Ministry of Health, Health Information Systems Yearbook, 2020)

It is a result that is likely to be met at the rate that can be predicted in Figure 9. Between 2016 and 2021, a maximum of 112 emergency ambulances were used. In the light of these figures;

- The most accidents occurred in 2021 because the number of injured increases more than in those other years.
- The highest death rate was in 2016 because it is thought that traffic education has increased in 5 years.
- It has been observed that the highest number of accidents occurred in 2021 with traffic collisions. The reason is thought to be due to the emptiness of the streets due to the effect of the pandemic and the fact that people pay less attention to the rules in empty streets.

DISCUSSION

The authors presented an index (Efficiency Index) to objectively measure the effective implementation of an Occupational Health and Safety Management System (OHSMS). The article shows how the index can be applied practically to a company and what kind of information can be collected and processed to determine the effective implementation of the OHSMS. The document also aims to define a procedure for demonstrating that a company is exempt from liability in the event of an unforeseen accident and to allow for a further reduction of insurance premiums. In fact, only the exclusion of employers from liability through

the effective implementation of the OHSMS combined with an adequate incentive policy can significantly improve occupational health and safety. The article shows how the index can be applied practically to a company and what kind of information can be collected and processed to determine the effective implementation of the OHSMS. The document also aims to define a procedure for demonstrating that a company is exempt from liability in the event of an unforeseen accident and to allow for a further reduction of insurance premiums. In fact, only the exemption of employers from liability through the effective implementation of the OHSMS in conjunction with an adequate incentive policy can significantly improve occupational health and safety (Bianchini, 2017).

The first priority of emergency medical services (EMS) is safety. Ambulance accidents not only delay patient transfer, but can also endanger ambulance passengers and other road users. However, this important question of patient and provider safety often goes unexplored in high-income countries (HICs). EMS (emergency medical services) vehicle accident investigation is even less common in small and medium-sized countries. The officially established EMS system in Thailand, where the risk of motor vehicle collisions is high and the conditions are completely different, includes hospitals, cities and volunteers. All of them consist of ambulance teams managed by command and control centers located in provincial hospitals or provincial health departments. Hospitals usually include advanced emergency medical technicians (EMT), paramedics, nurses, or emergency room doctors who provide pre-hospital care; Volunteer or municipal teams, including primary emergency medical responders or emergency medical first responders (EMRs), provide primary care. Receiving an emergency call from the national emergency ambulance number (1669), the control tower dispatches a suitably skilled ambulance crew from the nearest location. EMS in Thailand implements a number of safety measures, including ambulance speed limits, driver training, and established procedures for the use of safety devices. However, 61 ambulance accidents were reported in 2013, including 130 injuries and 19 deaths. To elucidate modifiable risk factors for ambulance accidents and resulting injuries, this report presents a case of an ambulance accident, an LMIC in Thailand (Pattanarattanamolee, et al., 2017).

When looking at other countries, it is determined that this situation varies depending on the development level of the countries. In other words, since the health systems of developed countries have also developed, they will give priority to the primary health care system, and they are in a better and equipped position in terms of emergency response. Not only in the treatment part, but also in terms of occupational accidents, being more obedient to the rules prevents ambulance accidents. Likewise, in

developing countries such as Turkey, primary care is neglected as this situation will prioritize tertiary health care rather than primary care, and this situation can force the emergency team. In addition to this, since the compliance of the developing countries with the rules will be low, the possibility of increasing occupational accidents is also seen.

While vehicle accident investigation is even less common in Thailand than in small and medium-sized cities, a country-wide system prevails in Turkey. When examined in terms of working hours, it is observed that individuals who work long working hours may cause neurological and cardiovascular diseases. In different studies conducted in Europe, it has been determined that more invitations to work accidents are prepared after working hours exceeding nine hours. This situation is valid for Turkey and even for the whole world. In the United States, a labor statistics report was prepared on this subject in 2012. According to this report, it has been determined that the number of days spent away from work and reports including non-fatal accidents and occupational diseases are higher in prehospital emergency health workers than other health workers (24% higher than the group such as nurses, nurse assistants, home caregivers). (Yıldırım and Gerdan, 2017).

CONCLUSION AND RECOMMENDATIONS

Health professionals working in Emergency Service Stations and Ambulances, assuming that Vehicles and Ambulances meet the standards of the Regulation, require that they know and practice occupational health and safety very well in order to identify the dangers and risks they encounter as a result of their work and to prevent work accidents and occupational diseases that they may encounter. Prioritizing the risks that may arise as a result of this, taking precautions and in this direction, being able to solve possible problems in advance will reduce the risk factor.

Due to the existence of the concept of occupational health and safety, it aims to protect every individual against every working condition, even in the smallest problem. In particular, healthcare workers are the occupations that are at the greatest risk in this regard. The risk factor also increases among health personnel. In particular, we have personnel using group ambulances that meet this requirement. Because this group is the group that encounters traffic accidents the most. In the light of the data obtained as a result of this study, ambulance workers in the risk group should be informed about occupational health and safety. Because the employee who receives training is expected to be conscious and it is expected that he will use the training he has received and protect himself. At the same time, it is extremely important to give traffic rules and attention training to ambulance workers. Because an ambulance that complies with the traffic

rules reduces the risk of accident. Likewise, since most of the accidents are caused by attention, reducing the accidents can proceed in direct proportion to reducing the attention.

There are many known and unknown causes of traffic accidents, and based on the known causes, it has been reached the data that the accidents are mostly caused by taking the wrong road. It is thought that this situation was observed especially in 2020 and after, because the streets were empty due to the pandemic at that time, and this resulted in the drivers neglecting the rules. This situation shows that developing countries such as Turkey are not binding on the rules. As a result, it is concluded that this situation caused the accident.

One of the most important risks for people working in pre-hospital health services is compassion fatigue and post-traumatic stress disorder. High volume visits, prolonged working conditions, the potential for violence and high work stress, frequent increases in anxiety or depression, poor job performance and quality of worker lives increase. Especially in the summer months, working overtime and not being able to provide the necessary health personnel for emergency aid, not consuming work permits increases the number of cases and causes an emergency medical situation before admission. As a result, caregivers become psychologically exhausted. This attrition is patient-centered and can lead to neglect. It is also the source of many employee-centered problems arising from accidents and diseases. According to the working regime, 3 meals a day and 2 hours shift support should be provided by the general and service sector. As a result, it is a factor in ambulance accidents, so these issues should be taken into consideration.

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CHAPTER 8

INFERTILITY AND PRENATAL ATTACHMENT

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INTRODUCTION

The World Health Organisation defines infertility as a disease of the reproductive system defined by the inability to achieve pregnancy after 12 months or more of regular unprotected sex. The global prevalence of infertility is approximately 50-70 million couples, these numbers show us how many people are affected by this condition (Mascarenhas et al, 2012). Infertility is estimated to affect up to 186 million people worldwide. The recommended evaluation for patients presenting with infertility is to evaluate women who cannot achieve pregnancy after 12 months of unprotected sexual intercourse. For women over 35 years of age who have been unable to conceive for 6 months, early evaluation is recommended; urgent evaluation is required for women over 40 years of age. Evaluation is also recommended for women with oligomenorrhoea or amenorrhoea, known or suspected uterine, tubal or peritoneal disease (including stage III or IV endometriosis), and known or suspected male infertility. (ACOG,2014)

Approximately 1 in 8 women aged 15-49 receive infertility services. Although success rates vary by age and diagnosis, shared decision-making with accurate diagnosis and effective treatment can enable many couples undergoing infertility treatment to achieve their fertility goals. (Sandra, 2021)

Prenatal attachment is defined as “an abstract concept related to cognitive and emotional abilities to conceptualise another human being, which represents the filial relationship between a pregnant mother and her foetus and can begin even before pregnancy”, which is one of the most recent definitions proposed by Doan and Zimmerman. (H.M. Doan , A. Zimmerman 2003).

Behaviours such as imagining the baby, paying attention to the mother’s nutrition, avoiding alcohol and smoking, talking to the baby, preparing the house, choosing a name, buying clothes and learning the process are part of the concept (Cranley, 1981). Prenatal attachment is not a static process, it is a process that develops and transforms as the pregnancy progresses. Prenatal attachment has a key role in maternal identity and has an effect on the mother’s positive adaptation to the postnatal period (Pisoni et al. 2016).

Attachment begins to form when the mother learns about her pregnancy and starts to bond with her baby. The mother’s interaction with her baby after birth and her motherhood experience are linked to the bond that develops between her and the baby during pregnancy and the emotional health of this pregnancy (Elisa et al 2021).

The relationship established between mother and child in the early period of life is very important as it serves as a prototype for various relationships in the later stages of the individual's life. In recent years, there has been an increase in studies on the mother-infant bonding (Dubber et al. 2015) If we are to give examples of studies on prenatal attachment,

Kumar (1997) and Marsh (2007) concluded that anxiety or depression during pregnancy and postnatal period prevents mothers from establishing a full bond with their babies (Kumar 1997, O'Keana & Marsh 2007) Goecke et al. (2012) found that women with low depression scores during pregnancy had high quality prenatal attachment.

Infertility is a highly stressful situation and can be defined as a crisis that affects various aspects of the lives of infertile couples. Infertile couples experience many negative emotions such as anxiety, depression and guilt and become prone to mental problems. The results of the study show that pregnancy through an ART for women and men who have been previously affected by infertility has different levels of repercussions on their relationships with other people as well as in couple relationships (Fisher, 2008).

In some studies, mothers who participate in educational activities exhibit more maternal behaviour and this may positively affect their health. Educational interventions may be a predictor of mother-infant attachment, the primary relationship between mother and infant. Thus, increased attachment during pregnancy leads to more self-confidence in assuming the role of motherhood and contributes to the mother's greater adaptation to postnatal conditions and positive reactions to the baby's behaviour (Toosi, 2017).

In the study conducted by Kavlak et al. in 2020; prenatal attachment was examined in women who conceived after infertility treatment, and as a result, it was observed that the mean PBE score was lower than that of women who conceived spontaneously (Kavlak et al., 2020) In Karaahmetoğlu's master's thesis study in 2021, it was observed that there was no significant difference between the level of prenatal attachment when the risky pregnant woman was taken as the main factor in determining the level of prenatal attachment in high-risk and low-risk pregnant women. (Karaahmetoğlu, 2021) Toosi et al. showed that relaxation training was effective in reducing anxiety and increasing maternal-fetal attachment in women undergoing ART for conception (Toosi et al., 2017).

A literature review included cross-sectional and longitudinal studies published between 1990 and 2019. A search was performed using MEDLINE/PubMed, EMBASE, Web of Science, Scopus and Google Scholar search engine. 15 articles were included and the findings showed

that infertility problems did not affect prenatal attachment after ART. However, research findings indicate that ART couples may be more prone to anxiety due to pregnancy loss (Ranjbar, 2019).

The Importance of Nurses in Prenatal Attachment in Infertile Groups

Menning (1977) defined infertility as a life crisis, a period of instability. It may reawaken unresolved psychological problems from the past and may lead to cycles of hope, loss and despair. (Menning, 1980).

In order for the attachment between mother and baby to be secure and positive parenting behaviours to be adopted, counselling services should be provided to women from the gestation period (Akarsu et al., 2017). The findings obtained in many studies show that the importance of nurses and other health professionals providing care to this group cannot be denied. Couples who were previously affected by infertility and conceived with ART are under the influence of many negative factors related to the difficult and uncertain treatment process (René et al. 2022) are a group that needs more support.

After the pregnancy occurs, the nurse should support the mother to feel her baby, accept the changes in her body and transfer them to her baby with positive emotions. The best time period to evaluate this process is pregnancy follow-up. Careful follow-up of prenatal tests, necessary treatment and care by the nurse in routine controls will facilitate a pregnant woman's adaptation to pregnancy (Koç et al., 2016; Tunçel et al., 2019). Mother and father should be informed about issues such as mother-father-infant communication, factors that increase and affect attachment, baby care, parenting behaviour in prenatal, birth and postnatal period (Bağrıyanık et al., 2020). Evidence-based practices can be used to determine and increase the level of anxiety and attachment in risky pregnancies such as infertility and to reduce anxiety (Baltacı & Başer, 2020). Prenatal trainings, one of these, have been found to positively affect mother-baby attachment and reduce the stress level of mothers (Tunçel et al., 2019).

Prenatal education, allowing the mother to visualise her unborn child and providing more information about fetal development are important to ensure early maternal-fetal attachment in women pregnant with ART. Therefore, providing social support to women pregnant with ART is very important in the development of maternal-fetal attachment (Kuo, 2013).

Conclusion

Infertility and its treatment are very complex processes that affect many areas of an individual's life. Therefore, couples affected by this

situation remain in different emotions and situations while experiencing the pregnancy process. In addition to the psychological effects of a difficult pregnancy and the process of achieving a much desired baby, it also directly affects prenatal attachment. Therefore, providing special training and counselling especially for this group will contribute to the healthy overcoming of this process and the development of positive attachment processes.

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CHAPTER 9

3D PRINTING IN ORTHODONTICS

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Introduction

The steps involved in 3D printing an object are collecting relevant data, creating a 3D file from that data, and finally printing the file using printing machines (Piedra-Cascón et al., 2021). The process of creating a physical object from a digital three-dimensional file using a printer is known as 3D printing. 3D printing is also known as additive manufacturing and rapid prototyping (Liu, Leu, & Schmitt, 2006; Yan & Gu, 1996).

The first documented iterations of 3D printing can be found in Japan in the early 1980s. Hideo Kodama was looking for a way to develop a rapid prototyping system in 1981. He created a layer-by-layer fabrication method using a photosensitive resin polymerized with UV light (Kodama, 1981).

In 1983, Charles Hull invented the process of stereolithography, which is the first practical method for producing 3D objects from digital data (Zaharia et al., 2017).

Carl Deckard patented powder-based selective laser sintering (SLS) in 1989, which involves melting and re-fusing powdered material with a laser beam (Deckard, 1989).

Scott Crump introduced the technology based on the principle of melting thermoplastic filaments in FDM (Fused Deposition Modeling) style and forming them layer by layer on the production table in 1992 (Gross et al., 2014).

Advances in resin chemistry, parallel to advances in digital impression technology, have increased the use of 3D printing technology in dentistry (Panayi, Cha, & Kim, 2023). With this cutting-edge technology, working models, prosthodontic restorations, orthodontic appliances, surgical guides for implant placement, and maxillofacial prostheses can all be manufactured (Fekonja, Rošar, & Drstvenšek, 2019; Graf, Tarraf, & Kravitz, 2021; Graf, Tarraf, & Vasudavan, 2022; Grauer et al., 2012; Panayi et al., 2023; Rajasekaran & Chaudhari, 2023; Tsolakis, Gizani, Tsolakis, et al., 2022; Wu, 2022). The proliferation of AI-assisted CAD software is significantly transforming the 3D printing landscape. Leveraging AI-driven algorithms in the preparation and conversion of 3D models has led to faster workflows and enhanced model quality. AI has proven effective in various aspects of the process, including printability assessment, slicing optimization, nozzle trajectory planning, and cloud-based services (Fiedor & Ortyl, 2020). Furthermore, artificial intelligence segmentation of CBCT DICOM files in a short time, examining bone-tooth, tooth-tooth, and upper and lower jaw relations on the model with the patient outside the mouth, and including the patient in treatment plans are important developments (Cui et al., 2022). All these developments can be predicted that Dentistry will be one of the professions that benefit most from 3D printing technology and undergo changes due to these developments.

One of the areas of specialty most affected by 3D printing in dentistry is orthodontics. All orthodontic applications, whether fixed metal applications or removable plastic and acrylic appliances, benefit from 3D printing technologies in orthodontics (Graf et al., 2021, 2022; Rajasekaran & Chaudhari, 2023; Yang et al., 2012). With CBCT, creating a patient treatment plan based on the use of intraoral and laboratory scanners, designing the appropriate appliance, simulating the course of treatment to the patient, or showing them by printing are important gains of digital dentistry.

This chapter discusses the use of 3D printing technology in orthodontics, specifically in the production of clear aligners. Align Technology is highlighted as a prominent example of this technology, which uses an indirect approach to fabricate aligners (Kuo & Miller, 2003). The document also notes the increasing use of resin-based printers and special printer technologies that print hard materials like metal and zirconium in orthodontic treatments (Tsolakis, Gizani, Tsolakis, et al., 2022). Finally, the chapter lists several common 3D printing technologies used in orthodontics, including selective laser melting, stereolithography (SLA), digital light processing (DLP), and liquid crystal display (LCD)

Selective Laser Melting (SLM)

A powerful laser beam is used in SLM to create 3D metal parts or appliances. During the printing process, the laser beam melts and combines various metal powder particles. When a thin layer of material is in its direction, the laser beam selectively unites or welds the particles. This method is repeated until the appliance is created, layer by layer (Gokuldoss, Kolla, & Eckert, 2017).

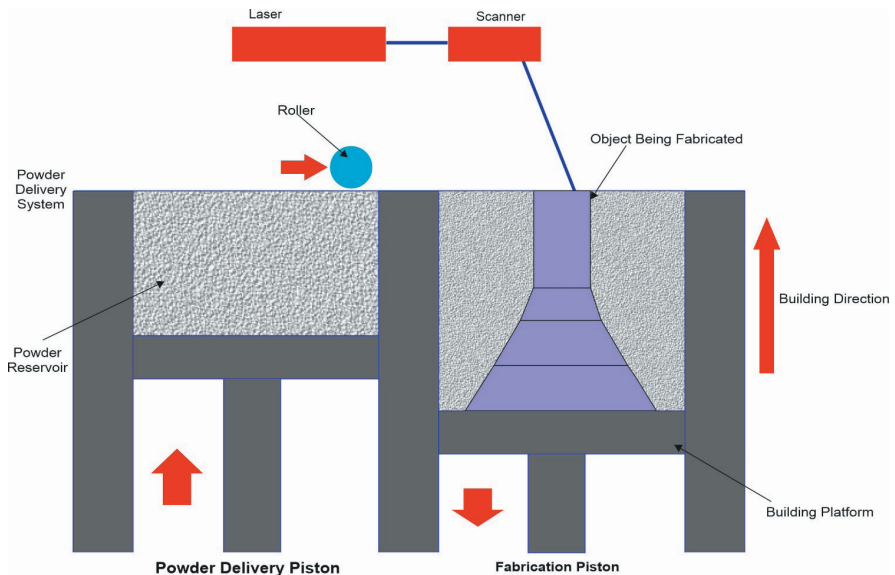


Figure 1: Illustration of SLM

Support structures are necessary to prevent the collapsing of the linked particles during printing. An unfinished body with these support structures is produced following the printing process. For these reasons, post-print processing is applied to the printed item.

The post-printing process entails removing excess powder particles and supports, but since the support structures of metals must be properly removed, it is significantly more difficult and often requires a CNC machine (Panayi, 2021).



Figure 2: Printed Part with Rough Surface

Orthodontists can benefit from selective laser melting (SLM) to create custom metal appliances for patients, such as rapid palatal expanders (RPE), molar distalization, and anchorage retaining appliances. Patient-specific components offer many benefits, including improved precision and comfort.

The greatest advantage of direct metal printing is the ability to create highly personalized devices with numerous design options. Orthodontists can design the appliance for its intended function using an appliance design program on their computer, or they can send intraoral scans directly to the laboratory to collaborate with the technician on appliance production. This method eliminates the need to separate the molar teeth and standardizes production, reducing the technician's manual skill requirements.

Ultimately, this procedure prioritizes the patient's comfort, making it a preferable alternative to conventional techniques for applying appliances (Graf, 2018; Graf et al., 2021).

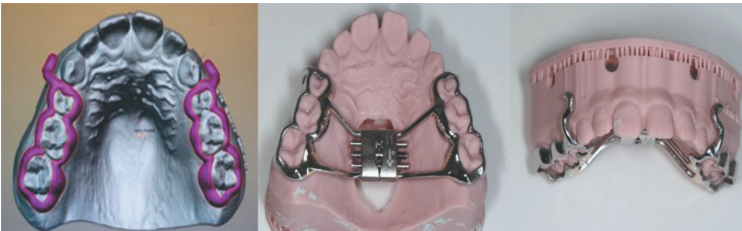


Figure 3: From Design to Print Orthodontic Appliance.

FDM (Material Extrusion)

FDM (Fused Deposition Modeling) 3D printers use thermoplastic filaments to create objects by melting the filaments and layering them on a production table. The technique is based on Material Extrusion and involves continually extruding a plastic filament in the shape of a cable through a heated nozzle. The printer deposits each layer on the production table, and the nozzle and platform can move horizontally and vertically, respectively (Lin et al., 2019).

While FDM technology is utilized in dentistry to produce surgical guides, orthodontic models, and educational models, it produces less accurate prints than other additive manufacturing technologies (Kim et al., 2018; Rouzé l'Alzit et al., 2022). The accuracy and speed are low due to the material-depositing nozzle's radius, and the quality of the finished product is limited by the nozzle's thickness. The most commonly used polymers in FDM technology are ABS (acrylonitrile-butadiene-styrene), PLA (polylactic acid), and PET-G (polyethylene terephthalate glycol).

This printing technique is cost-effective and requires minimal post-processing, such as removing supports and smoothing the product. Although FDM printing is not common in orthodontics, it is widely used in producing educational models and slightly in thermoformed clear aligner production (Jaber et al., 2021).

Vat Polymerization

Vat polymerization is the process of building the model layer by layer from a vat of liquid photopolymer resin. UV (ultraviolet) light at a certain wavelength can be used to cure or harden the resin as needed. Upon the completion of each subsequent layer, the object is lowered from a platform. SLA, DLP, and LCD printers all exhibit vat polymerization (Dufera Tolcha, Srinivasulu Reddy, & Dufera, 2019; X. Xu et al., 2021). These technologies use light to cross-link chemical monomers and oligomers. The result of this process is the formation of polymers that form a three-dimensional body. The most commonly used material by this technology are mixtures called “resins.”

FEP (Fluorinated ethylene propylene) film used in vat polymerization separates the liquid resin and build plate from the light source of the machine, allowing UV rays to enter and cure the resin. Replacing FEP film when it becomes bent, deformed, or perforated is essential to ensure successful printing.

Slicer Programs

The process of preparing a digital three-dimensional model for actual 3D printing is referred to as “slicing” in 3D printing. Slicing software serve as a bridge between the CAD and printed object. Objects imported these programs in STL format are organized and opened in printer-specific slicing programs or open-source programs such as Chitubox (Chitubox, China) and Lychee (Mango 3D, France). Objects are organized according to the size of the printer.

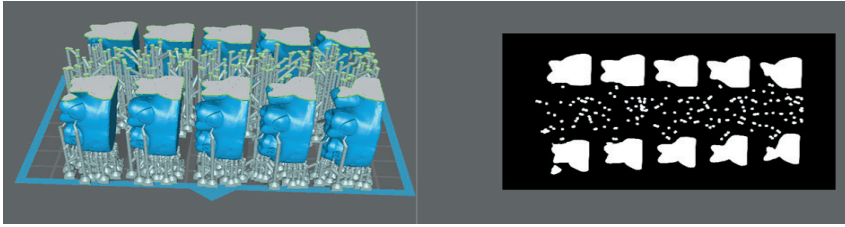


Figure 4: Sliced Dental Models.

Depending on the intended use, dental models are typically arranged either vertically or horizontally. In orthodontics, models generally are vertically placed to accommodate a larger number of models. When the models have been aligned, a variety of supports are created to prevent the structure generated during the printing process from collapsing (Panayi et al., 2023).

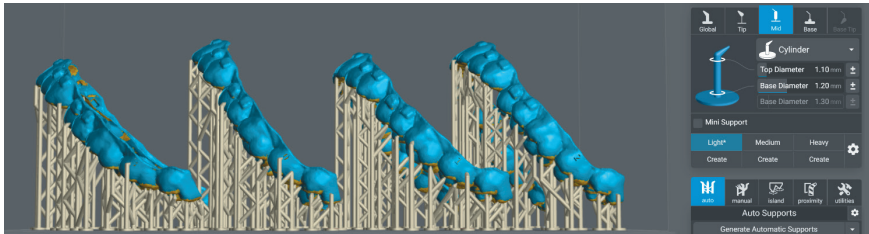


Figure 5: Designing Support Structures

After the object or objects have been prepared for printing, the software automatically slices the STL file, with each slice indicating the cross-sectional layer that must be cured. Each image represents a layer successively projected to form the structure of 3D object. Several slicing programs for 3D printing have tools for creating hollow 3D models, reducing the amount of resin needed for printing. Users need to keep in mind that if they intend to print hollow models, they will need to include drain holes in order to avoid the resin from getting stuck. The slicing algorithm, which is controlled by the printer software, divides the object into slices of equal thickness based on the STL file-specified surface of the 3D object. The slicing program regulates all fundamental printing settings, including the generation and positioning of support structures.

Manufacturer recommendations for the resins and printers to be used must be followed when adjusting the layer height, exposure duration, and other variables. The print speed and quality can be customized using these settings. When working with non-professional printers that have not been calibrated by the manufacturer, the user should generally begin with a test model to determine the optimal setting parameters before using the printers and resins to print any orthodontic appliance.

SLA

SLA is the oldest method of 3D printing. It is still commonly used and produces extremely precise and accurate prints. Stereolithography (SLA) is a method of additive manufacturing that belongs to the family of vat photopolymerization. Using ultraviolet lasers as a light source, stereolithography (SLA) selectively cures a polymer resin.

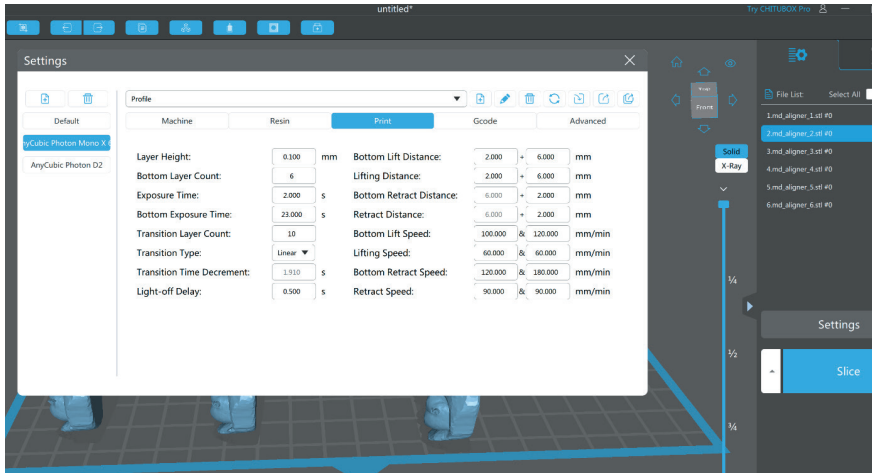


Figure 6: Configuring 3D Printing Settings

SLA

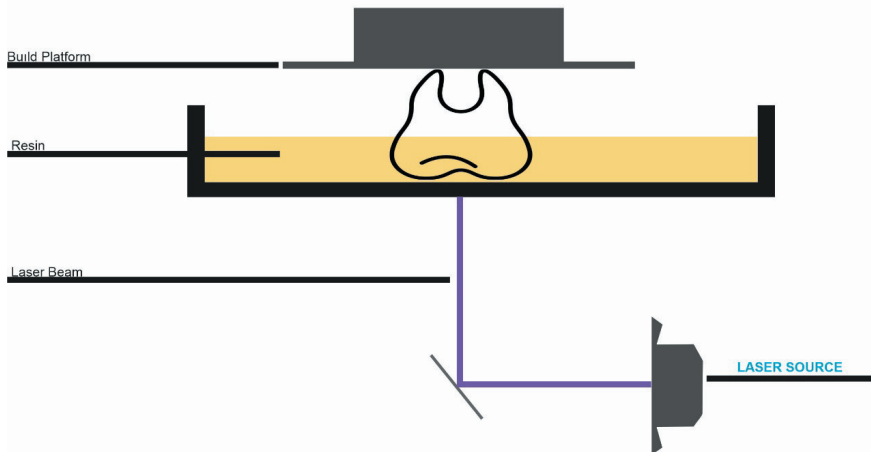


Figure 7: Illustration of SLA Printing

SLA 3D printing is accomplished by first putting the build platform in a tank of liquid photopolymer such that the first layer adheres to it. Based on this technology, the laser beam is positioned above the resin tank (Vat) and in an upward orientation. A group of mirrors called galvanometers directs the laser beam in a certain direction. The laser beam traces each point in a single layer of the resin

tank, solidifying the resin layer by layer. The platform descends layer by layer as the solidification process proceeds until a three-dimensional object is formed (Pillai et al., 2021). This printing process necessitated the development of a data transfer method between the computer and the printing device. Special STL (stereolithography) file formats were created for this purpose. STL is the native file format of 3D Systems' stereolithography CAD program (Gokhare, Raut, & Shinde, n.d.; Kessler, Hickel, & Reymus, 2020). The STL file format, which is widely used in 3D printing, has a variety of backronyms, including "Standard Triangle Language" and "Standard Tessellation Language" (Kessler et al., 2020). The STL format, with its various interpretations like "StereoLithography" and "Standard for the Exchange of Tessellation Data," plays a crucial role in digital manufacturing processes, such as 3D printing, by encoding objects as interconnected triangles or facets. In conjunction with this format, UV-sensitive photopolymer resins are used to create precise and intricate structures during the 3D printing process. These resins, which are photocatalyzed acrylic monomers, undergo crosslinking when exposed to ultraviolet laser light, thus enabling the successful transformation from digital models to physical objects.

DLP (Digital Light Processing)

The development of the DLP 3D printing method was a significant step forward in the evolution of 3D printing techniques. In digital light processing (DLP)-based 3D printing, projection light is used to polymerize materials and manufacture pre-designed models. DLP 3D printers create products on a build platform that is elevated above a vat of photosensitive resin. DLP printers employ a digital light projector screen to display cross-sectional slice of 3D Object. Each layer is built as the build platform slowly rises vertically from the resin vat. DLP uses a projector instead of a laser to create 3D objects. As opposed to SLA, the light does not only impact one spot when it hits the resin. Rather, the entire layer forms all at once (Scribante et al., 2022).

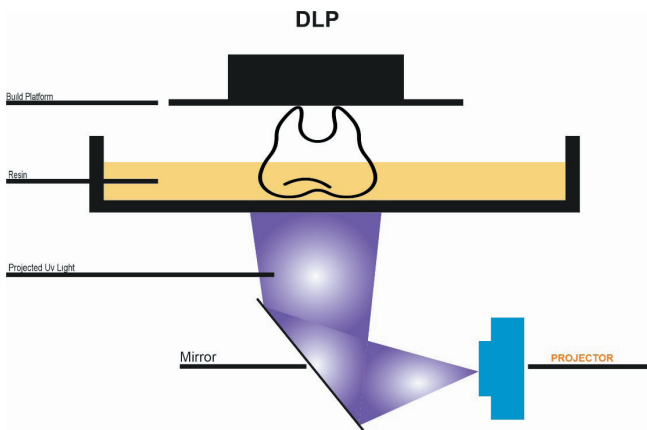


Figure 8: Illustration of DLP Printing

A DMD (Digital micromirror device) with hundreds of thousands of tiny mirrors directs light. A DMD builds the optical model for DLP 3D printing inside the projector lens. The DMD surface reflects light toward the liquid resin. The resin is exposed to and hardened by patterned light that is projected by a DMD (Digital Micromirror Device). Each mirror represents one or more pixels in the projected image. The number of mirrors corresponds to the resolution of the projected image (L. Hornbeck, 2009).

LCD (Liquid Cristal Display)

LCD 3D printing (also known as MSLA or Masked Stereolithography) is a relatively new technology that was created as a cheaper alternative to DLP and SLA. Instead of using mirrors, strong LCD monitors light the model with LEDs, which the LCD panel blocks off in the areas that are not to be cured (Lo Giudice et al., 2022). The LCD screen only lets the light pass-through areas that are to be cured into the finished part, simplifying the process, and removing the need for any mirrors or galvanometers. An image of each layer is generated on the LCD screen while an entire layer is hardened at once.

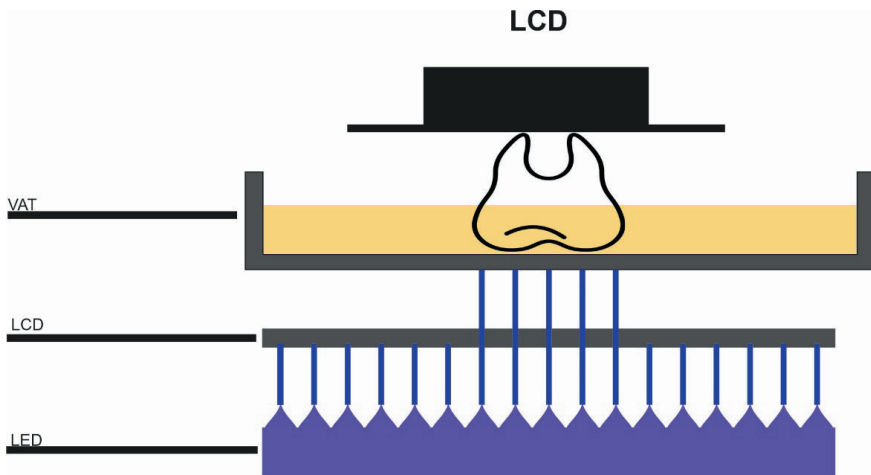


Figure 9: Illustration LCD Printing

The printing accuracy and precision of LCD printers are getting closer and closer to SLA and DLP printers (Nulty, 2022). The use of these printers is on the rise as they are inexpensive and produce acceptable prints for orthodontics and other dental applications (Tsolakis et al., 2022).

Post -Printing Process

The post-printing procedure consists of the removal of the support, the elimination of uncured resin, post-polymerization, and the polishing of

the object's sharp edges. Support elimination is a largely manual technique in which the tree-like support system of the printed product is eliminated, leaving behind an uneven surface.

Following the removal of supports, models can be cleaned of any residual uncured resin by rinsing them in an ultrasonic bath of isopropyl alcohol (above 91%) (Y. Xu et al., 2021), ethanol (99% (Lambart et al., 2022), or by using a centrifuge (Hertan et al., 2022). It is crucial to follow the manufacturer's recommendations for this operation. The model must be dried with compressed air after ultrasonic rinsing in a 2-stage cleaning process.



Figure 10: Cleani by Ackuretta - A Cutting-Edge Two-Stage Cleaning Unit
Figure 11: Graphy's Centrifuge Machine



Figure 12: Ackuretta's Polymerization Units (Curie, NFinity) and Graphy's Tera Harz Cure - Advanced Technologies for Efficient Curing Processes

Following the printing process, objects must undergo polymerization via ultraviolet (UV) curing. The equipment features specific settings tailored to various resins. As these settings can differ between machines, it is essential for users to adhere to the manufacturer's recommendations to ensure optimal results (Koenig et al., 2022).

Applications of Vat Polymerization in Orthodontics

Aligner Fabrication

There are currently two distinct types of aligner manufacture on the market. The first production is an indirect (thermoformed) form of aligner manufacturing, and this form of aligner manufacture is quite prevalent. Another option that has been popular in recent years is the manufacturing of aligners directly from a variety of resins (Bichu et al., 2023).

Indirect (Thermoformed) Aligner Fabrication

There are two ways that indirect aligner manufacturing occurs. Fabrication of aligners by companies and in-house aligner fabrication.

The process of creating clear aligners involves sending intraoral scans of patients to companies who use their own orthodontic software to create orthodontic tooth movements based on an orthodontist's prescription. The orthodontist can make modifications to the software and accept the final treatment plan online. Once accepted, CAD files are sent to SLA-type printers to produce dental models. The dental models are sprayed with a silicone release agent after printing to facilitate removal of the aligner during the forming process. These models are then used in an automated aligner-forming system where sheet plastic is heated, formed, and laser-marked. The aligners are trimmed by an automated cutting machine, polished, disinfected, and packaged before being shipped to the customer (Kuo and Miller, 2003).

In-house aligner manufacture differs from business production in that the majority of operations are performed by technicians or physicians utilizing primarily tiny printers (SLA, DLP, LCD) and thermoplastic forming machines. The procedure can be summed up as follows: scanning of the upper and lower jaws, preparation of a treatment plan utilizing multiple orthodontic programs, 3D printing, thermoforming, trimming and polishing, eventually packaging (Rajasekaran and Chaudhari, 2023).



Figure 13: Printed Dental Models

Aligner thermoforming is a process that uses vacuum or positive-pressure thermoforming equipment and thermoforming plastic sheets (Zendura; USA, Tristar; Malaysia, Taglus; India). To make accurate aligners, you need a thermoforming machine with enough pressure (Shah et al., 2022).

The thermoforming settings should be adjusted according to the manufacturer's instructions for the clear plastic sheet. The plastic sheet is softened with an electrically heated ring and then applied to the dental model. The air compression is activated, and it takes about a minute to mold the plastic with a series of lights to indicate time and temperature.

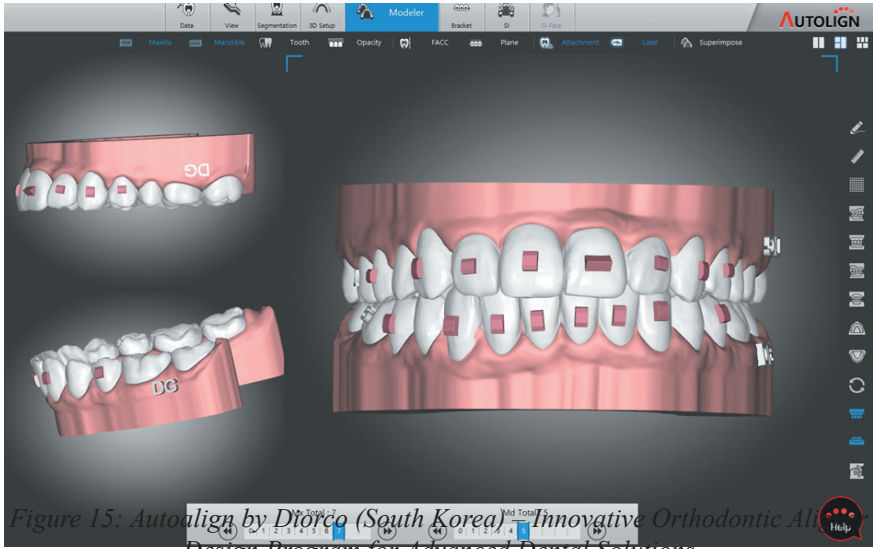


Figure 14: Ministar Thermoforming Machine (Scheu Dental, Germany)

The operator then removes the plastic, trim its margins, and polish the edges.

Direct Aligner fabrication

Direct aligner printing is a cutting-edge technique that has revolutionized the orthodontic industry. This method offers a host of innovations, including a significant reduction in the number of production stages required when compared to the traditional thermoforming method. Notably, this technique eliminates the need for dental models, which results in a significant decrease in the amount of resin used. While it is true that the cost of directly printed resin is currently high, it is expected to become more affordable as more companies enter the market and begin producing resin, driving competition and making prices more competitive.



The post-printing techniques employed by different resin manufacturers can vary significantly. For example, the earliest of these resins, Tera Harz TC-85DAC resin (Graphy Inc, Seoul, South Korea), has some unique requirements when it comes to removing uncured resin remnants. Specifically, it is recommended to avoid using isopropyl alcohol and ethanol to clean the models, as these solvents can negatively impact the resin's physical properties, including its durability.

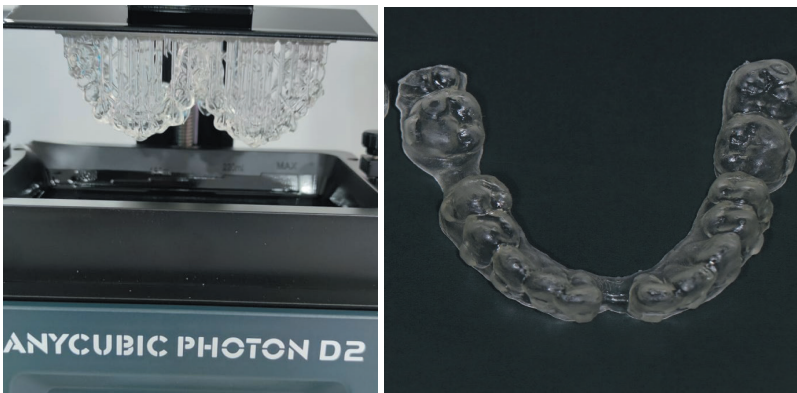


Figure 16: 3D Printed Aligners Using Anycubic Photon D2 DLP Technology

To properly remove uncured resin remains from models printed with Graphy's Tera Harz TC-85 DAC resin, it is recommended to use a centrifuge. In contrast, models printed with Clear-A resin (Senertek, İzmir, Turkey) can be cleaned using ethanol. If you are working with models

produced using OD-Clear TF ULTP resin by 3Dresynen, however, it is advised that you use Cleaning Liquid NW1 Bio (3Dresynen, Barcelona, Spain) to remove any uncured resin.

Fabrication Of Twin-block

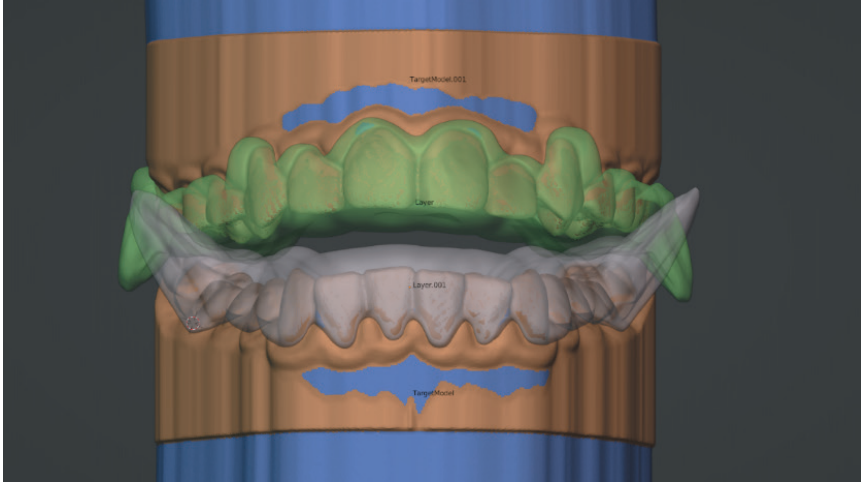


Figure 17: Twinblock Design by Blenderfordental

Such orthodontic appliances can be designed utilizing complimentary software solutions such as Meshmixer (Autodesk, USA) and Blender (Blender Foundation, Netherlands). Utilizing dentistry-specific modules in Blenderfordental (Blenderfordental, Australia) within the Blender program enables the efficient and effortless creation of these orthodontic devices. It is crucial that many laboratory-based processes are successfully moved to the digital realm and that the design is executed correctly. This program's articulator module simulates the condyle and enables the movement of the lower jaw. The lower jaw is repositioned after being protruded. Depending on the new position of the jaw, the lower and upper jaws are redesigned. This category of home appliances can be manufactured in two distinct methods. Similarly, to how aligners are manufactured, a clear sheet is printed on the lower and upper jaw models using the thermoforming method. Instead, the upper and bottom components of the Twin-block appliance are manufactured utilizing directly printed polymers (Panayi, 2021; Graf et al., 2022).

3D printing has undoubtedly revolutionized orthodontics, enabling the production of various appliances such as indirect bonding trays, mini-screw guides, orthognathic surgical splints, and occlusal splints. This cutting-edge technology has significantly improved the precision, customization, and efficiency of dental appliances, providing numerous benefits for both patients and dental professionals alike.

The general process for creating these appliances may be similar, but each one demands particular attention to its specific design and function. Orthodontic appliances serve different purposes, and it is crucial to consider the individual requirements of each patient when designing and fabricating these devices. The 3D printing process typically involves digital scanning, computer-aided design (CAD), and computer-aided manufacturing (CAM) to produce an accurate and customized product.

Selecting the appropriate resin based on the appliance's unique properties is crucial for optimal performance and durability. There are several types of resins available, each with their own characteristics, such as strength, flexibility, and biocompatibility. Some popular resins used in orthodontics include photopolymer resins, thermoplastic resins, and ceramic-filled resins. Dental professionals must carefully evaluate the specific needs of the patient and the appliance to determine the most suitable resin for the job.

Ensuring that 3D printed orthodontic appliances are biocompatible and non-toxic is of utmost importance to avoid any potential harmful applications. Biocompatibility refers to the ability of a material to coexist with human tissue without causing any adverse reactions, while non-toxicity ensures that the material does not produce any harmful substances. Dental professionals should stay informed about the latest research on biocompatible materials and 3D printing techniques to maintain patient safety.

As 3D printing technology continues to evolve and improve, it is essential for dental professionals to keep abreast of new developments and best practices. This includes advancements in materials, software, hardware, and overall techniques for creating dental appliances. By staying current on the latest innovations, dental professionals can ensure they provide their patients with safe, effective, and customized dental solutions.

In conclusion, 3D printing has already made a significant impact on the field of orthodontics and is poised to play an even more prominent role in the future. By understanding the unique design and functional requirements of each appliance, selecting the appropriate resin, and ensuring biocompatibility and non-toxicity, dental professionals can harness the full potential of 3D printing technology to provide patients with the best possible care. As the technology continues to evolve, it will be crucial for practitioners to stay informed and adapt their practices accordingly, ensuring the ongoing safety and satisfaction of their patients.

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CHAPTER 10

SPINE STRENGTHENING TECHNIQUES: VERTEBROPLASTY-KYPHOPLASTY

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Osteoporosis is a very common metabolic bone disease and decreases the bone mass, increasing the risk of fracture. A decrease in bone mass is also inevitable with aging. This risk increases rapidly in postmenopausal women. Approximately 3% to 16% of women and 1% to 8% of men over the age of 50 are affected. This rate increases in direct proportion to age. (2) An average of 750,000 osteoporotic vertebral fractures are observed annually in the United States.(3) These patients may require extended periods of hospitalization. Some of these patients have to continue their lives dependent on others. The primary goal should be the prevention of osteoporosis in order to reduce osteoporotic compression fractures. Medical treatment for osteoporosis significantly decreases the risk of fracture, making the identification of patients with risk factors and their treatment before a fracture occurs the most logical and inexpensive treatment.(4) Even if no neurological deficit is observed in patients with fractures, potential problems include severe low back pain and back pain, limitation of mobilization, and secondary pulmonary complications due to immobilization. Although the condition is not fatal by itself, the mortality can be increased due to the secondary complications. Some patients lose their ability to mobilize independently. Reducing the pain of patients with fractures and supporting their ability to stand up and mobilize as soon as possible are therefore very important. Classically, the treatments performed after a fracture can vary from conservative treatment to open surgical treatment. Classic treatment can be summarized using a brace, rest, and analgesia followed by medical treatment for osteoporosis. However, this approach does not give satisfactory results in some of the patients due to the increase in muscle atrophy and the secondary complications mentioned above caused by staying immobile. As regards the alternative treatment method of open surgical fixation, the age, poor health, and the fact that the patients are often too osteoporotic for bone stabilization with a pedicle screw can be considered the disadvantages. Therefore, minimally invasive spine strengthening techniques have emerged as a life-saving alternative for these patients in recent years.

Vertebroplasty is a percutaneous technique that was first used by Galibert et al. for a cervical hemangioma in 1984.(1) There was a significant decrease in the pain afterwards. Bone cement (polymethylmethacrylate) was found to contribute to the mechanical stabilization of vertebrae. The fact that the procedure is minimally invasive and often does not require general anesthesia, together with the short hospital stay, has led to its widespread use. It can technically be summarized as the injection of PMMA in a semi-fluid state with a cannula inserted through the vertebral pedicle into the anterior third of the broken bone's corpus. BU CUMLEYE BAKIN The development of paresis-plegia as a result of the leakage of

cement from the vertebral corpus into the spinal canal during this injection as well as severe pulmonary embolism after venous leakage and subsequent death have been reported.(5) These potential complications are the weak aspects of the technique. The kyphoplasty technique was developed by Mark Reiley in the United States in 1998 to avoid these complications. (5) This technique is similar to vertebroplasty in general and contributes to decreasing the complications and restoring the spine height as much as possible while correcting the deformity. PMMA is injected into the vertebral body, similar to vertebroplasty. In contrast, a working cannula is placed before the injection, balloons are inflated, and PMMA is injected into the formed cavity. This technical difference allows more dense cement to be injected and the injection can be performed in a more controlled manner with less pressure. The feared major complications of cement leakage into the spinal canal and pulmonary embolism are therefore decreased. The technique also provides a mean improvement of 14% in the sagittal plane in the correction of the spinal deformity.

DIAGNOSIS

First of all, a good history and physical examination are required. A history of trauma or systemic disease such as multiple myeloma or tumor that can cause a compression fracture should be queried. A history of osteoporosis and whether it has been treated, and whether the pathology has developed before or after the menopause in female patients should also be questioned. Then, a physical examination should be performed. Following a detailed neurological examination, the presence of pain when pressing on the spinous processes should be checked during palpation. Most of these patients experience pain at the level of the fracture with pressure on the spinous process. This pain is limited to the relevant point, and present in 90 percent of the patients. However, there may be no sensitivity with pressure in 10% of the cases.(7) The pain usually lasts for 4 to 6 weeks in the acute process. Chronic pain is present in a third of the patients. It is usually seen when the compression increases and more than one vertebra are involved.

1- Direct Graphs: Compression fractures are seen at the anterior-posterior and sagittal planes.

2- Computed tomography: The technique provides important information to determine the injection angle, pedicle thickness, and needle diameter, and also to evaluate the vertebral corpus in detail to decrease the risk of leakage. It also provides information during the preoperative evaluation regarding possible canal leakage by evaluating the corpus posterior wall. It is used to compare the pre-procedure and post-procedure status.

3- MRI: The differentiation between acute and chronic lesions is helped by the information obtained from MRI. Bone edema is an indicator of acute fracture and can be seen with STIR (short tau inversion recovery) sequence MRI. Besides, information on the differentiation of other pathologies that may be the cause of the pain (disc herniation, narrow canal, listhesis, spondylodiscitis, etc.) can be obtained.

INDICATIONS-CONTRAINDICATIONS

These are similar for kyphoplasty and vertebroplasty. The most patients are osteoporotic compression fractures, tumors and hemangiomas. Vertebroplasty can be performed to support the pedicle screw during surgery.

Neural deficits that correspond to the lesion area, canal compression, infection in the area of future intervention, a bleeding diathesis that could prevent the procedure, pregnancy, and iodine-gadolinium allergy may be listed as the contraindications in general. Fractures of the posterior vertebral wall, vertebra plana, and fractures above the T5-6 level have been considered contraindications in the past but the procedure can now be performed safely in these patients in experienced hands.

Kyphoplasty, unlike vertebroplasty, contributes to the correction of the height loss and kyphosis by inflating the bone with the help of a balloon. It is possible to decrease the kyphosis and height loss with kyphoplasty in fractures of less than 3 months in general, while the height loss can only be minimally corrected in longer fractures. The reason is prevention of the balloon inflation in intraosseous healing tissue by the remodeling process in fractures after 8-12 weeks.

TECHNIQUE:

Preoperative preparations for anesthesia for both techniques are the same as if open surgery will be performed under general anesthesia. Although the procedure starts locally, it should be noted that emergency decompression surgery may be required in case of canal leakage,. The surgical and anesthesia team therefore need to be prepared. We prefer local or sedation anesthesia under operating room conditions at our clinic. Surgeons who are new to the technique may prefer general anesthesia in patients with limited cooperation such as those suffering from dementia.

Once the patient is placed in the prone and neutral position, the relevant level is determined from the outside using a Kirschner wire laterally under fluoroscopy. Local anesthesia is administered approximately 4 cm lateral to the midline and the procedure is started. After passing the skin and muscle with the guide needle, the pedicle entry point is determined at 10 o'clock on the left and 2 o'clock on the right. During the scope evaluation, attention

should be paid to the absence of an oblique image in the lateral exposures, and the pedicles should be seen one by one and on top of each other at the relevant level, with no double pedicles present. The spinous process should be in the middle and the endplates should appear parallel on the anteroposterior radiograph. The lateral and anteroposterior graphs should be checked intermittently as the guide needle is advanced. The Kirschner wire is advanced once the previously advanced guide needle enters the corpus in the anterior-posterior image and lateral image. The Kirchner needle, which reaches the anterior third of the corpus in the lateral image, should be close to the midline but should not cross the spinous border on the anterior-posterior graph. If it has crossed the spinous border, there may be a risk of intracanal leakage since it would be close to the midline and the entry is medial. . If the Kirchner needle seems to have just entered the pedicle close to the lateral part and it is too close to the lateral wall of the corpus, it can be considered that the entry is too lateral. In this case, another attempt can be made. Once the procedure has been performed appropriately, the Kirschner needle is withdrawn and a biopsy is taken with the help of a drill. Although it is sometimes not possible to take a biopsy because the internal part of the bone is too hollow, we recommend a biopsy whenever possible. Osteomyelitis and tumor may be present in patients thought to have osteoporosis, and the pathology may also reveal an osteoporotic fracture following tumor treatment in patients diagnosed with a tumor (8). In addition to obtaining a biopsy, the use of drills creates a space in the vertebra and allows balloon placement. We generally implement this procedure transpedicularly on both sides for the lower thoracic and lumbar regions at our clinic. However, since we perform the intervention extrapedicularly in the upper and middle thoracic regions, the closeness of the needle to the midline is more suitable for this intervention. A unilateral approach is therefore generally adequate. An extrapedicular intervention is used in the thin middle and upper thoracic region to prevent the risk of pedicle fracture and medial neural tissue damage. If the intervention is bilateral, the balloons are inflated after the bilateral drilling procedure. The amount of inflation will provide a guide for the amount of cement to be used. It is important not to break the endplates while inflating the balloons. The balloons are deflated and removed once sufficient reduction is achieved. The 1.5 cc cannulas are then used for the injection. The maximum amount that can be administered is 1-2 cc more than the amount used for balloon inflation. The administration of PMMA in paste consistency is recommended. Bilateral filling should be targeted for both unilateral and bilateral interventions. Unilateral filling creates a risk of fracture on the other side. In case of leakage, the procedure can be stopped or it can be continued in a controlled manner after a while following slight withdrawal of the cannula. After the procedure is completed, a follow-up

CT or direct graph can be obtained and the patient discharged on the same day or the next day.

THE COMPARISON OF KYPHOPLASTY AND VERTEBROPLASTY

There is no significant difference between the methods in terms of pain palliation. A significant decrease in the pain is expected following both procedures due to the thermal and mechanical stabilization effect of PMMA. However, the cement can be administered with thicker consistency and at lower pressure with the kyphoplasty technique due to the balloon inflation. Therefore, the risk of cement leakage is lower. Besides, some reduction of kyphosis is provided and can prevent the related secondary complications(10). However, vertebroplasty is also effective for pain palliation and is a cheaper method.

COMPLICATIONS

The most common complication of these procedures is cement leakage. In general, anterior and lateral leakages are asymptomatic while posterior leakage may present with neurological symptoms. Kyphoplasty decreases the risk significantly with the use of thicker cement consistency and lower pressure.(10) Cement leakage is more common in malignancies. Although some cases improve with steroidal and non-steroidal anti-inflammatory drugs, others require surgical intervention.(12) Pulmonary embolism that can have a fatal outcome has also been reported after perivertebral leakage of PMMA.(11) The use of thick cement consistency and working on less than 3 levels in a single session are recommended to prevent this rare complication. An important point is the potential adjacent level vertebra fractures that may develop.(13) Leakage of cement into the disc space, loss of disc elasticity, and increased bone resorption due to the cement increase the risk of repeat fractures.

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CHAPTER 11

HEALTHCARE DATA SCIENCE AND EVALUATING THE IMPACT OF QUALITY/ PERFORMANCE/PROCESS IMPROVEMENT IN HEALTHCARE

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The aim of data mining in healthcare, is to identify useful patterns by analyzing large sets of data. These data patterns can predict number of patients and their characteristics and establish best practices on treatment, prevention, and self-care of patients.

With access to data related to individual patients, larger populations and their care, the hope is that public health professionals can analyze this combined data to improve patient outcomes with low costs. In the healthcare, data mining can be used to lower costs by increasing efficiencies, improve quality of life for the patients, and save the lives. There are three main topics in healthcare data science: Descriptive analytics, Predictive analytics, and Prescriptive analytics.

Modern healthcare analytics can be viewed as an integration of business intelligence, statistics, modelling, information systems, and optimization. The intersection of these areas is important as they can explain most real-world problems. Data mining focuses on understanding characteristics, detect anomaly's and patterns among variables in large datasets using various statistical and analytical tools.

Decision support systems by combining business intelligence concepts with operations research and management science to support decision making. It includes data management, model management and communication systems. Decision support systems is changing how healthcare managers make decisions with the tools and solutions from descriptive analytics, predictive analytics, and prescriptive analytics.

Descriptive analytics

Descriptive analytics uses the data visualization, dimension reduction, and exploration techniques to answer specific questions and to identify patterns. With the emerge of hospital information systems, and collection of electronic health records and clinical support systems, data availability increased drastically. Using these data sources effectively is challenging and at utmost importance. Descriptive analytics is the simplest and easiest way to explore the data to quantify events and report them in a human-readable way.

Descriptive analytics uses of data to evaluate performance and make well informed decisions. This is the most well understood and most common type of analytics. The techniques used for categorization, characterization, consolidation, and classification. Mainly data is converted to useful information. Descriptive analytics summarizes data into meaningful and explainable charts and reports. Basic visualization tools like bar charts, scatter plots, boxplots and histograms are main features used in descriptive analytics to expand the capabilities of these plots. Prediction,

classification, time series forecasting, and unsupervised tasks can be some other examples that can enhance visualization. All the tools in descriptive analytics are used to glean insights into benchmarks and trends.

Big data analytics tools have played a important role in healthcare decision-making. All data are captured digitally. Data have been growing at an exponential rate. Digitalized healthcare data is the massive amounts of data from various sources. This big data revolves around variety, volume, velocity and veracity. Big data come from many sources and very unstructured in nature and very messy. It requires sophisticated analytics to process the data and have meaningful conclusions from them.

In healthcare, predictor data sources can be public health, social media, clinical and internet data sources. Healthcare organizations keep record of the positive tested laboratory analysis of all specimens reported to regional, national, and international public health authorities. With the advancement of healthcare records, WHO is collecting all instances for a possible outbreak.

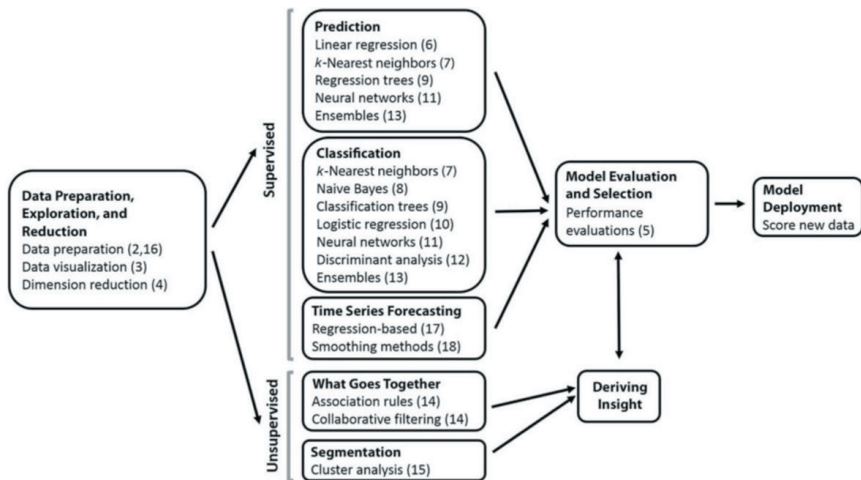


Figure: Data mining processes from Shmueli, *Data mining for Business*.

Predictive analytics

Predictive analytics commonly uses past data with statistical modeling to make predictions. The models created with predictive analytics are used to answer questions about the future. We can gain insight with predictive analytics. A mathematical model is built using the historical data to capture important trends. It is a great tool to suggest actions to take for the optimal outcomes. For instance, determining the number of new cases is perhaps the most important use case for predictive analytics during the pandemic. Predictive analytics forecasts by looking into historical data, detecting

patterns or interactive relationships. Predictive analytics can also predict risk and anomaly and hidden patterns. It can also be used to cluster data into cohesive subsets to forecast behavior and trends.

The workflow of the predictive analytics application follows four main steps. First step is data importation. Second step is data cleaning by removing outlier and combining multiple data sources. Third step is developing a high-performance predictive model based on combined data using statistics and machine learning. Last step is the integration the model into the forecasting system.

Regression analysis is a tool to build statistical models that characterize relationships between a dependent variable and explanatory variables. Two main categories of regression models are used often in healthcare analytics regression models of cross-sectional data and regression models of time series data. Linear regression models are the most common technique for the purpose of prediction. It is used for the purpose of inference and prediction. Explaining and quantifying the average effect of inputs on an outcome and predicting the outcome value for new records is the descriptive task and predictive task of the models respectively. In explanatory models, the objective is to fit the data. Thus, regression can be used for fitting and predicting.

For the fitting, it is best to the entire dataset. The performance of the model is evaluated by how the data fit into the model. Focus is on the coefficients. On the other hand, a predictive model forecasts new record. The performance measured by accuracy. The data is split into training and validation set. The test set is used to assess predictive performance. The model's performance is evaluated by its predictive accuracy and the focus is on the outcome variable.

K-nearest-neighbors algorithm can be used for prediction and classification. This method mainly is used for classification or prediction. Either categorical or numerical outcome can be generated. To classify a new record, the method looks for “similar” records in the training data. These “neighbors” are then used to find a class for the new record by using averaging for prediction algorithm. Main idea in k-NN methods is to identify k records that are close to the new record that is up for classification.

The Naive Bayes method is very common to classify. Principle is easy to follow. For each record, first find all the records with the same predictor profile and determine what classes the records belong to and determine the most common class. Finally, assign that class to the new record. It is very naïve but works great with nonhomogeneous sets. Obtaining class probabilities allows to classify a record as belonging to class P_i , even if P_i is not the most probable class for that record, this method has that flexibility.

There is also the very powerful classification method called logistic regression. Like linear regression, it is based on a model working with the relationship between the predictors with the outcome. The predictors must be specified. It works well with even small datasets. Main advantage is it is computationally fast and easy to classify large samples of new records.

Neural networks method can be used for classification, prediction, and feature extraction. It is the basis for deep learning. Many artificial intelligence applications like voice recognition uses neural networks. Main items can be listed as “nodes” and “layers”. The layers can be input layers, output layers, and hidden layers between them. This method is a Blackbox method.

The global healthcare predictive analytics market size was valued at USD 9.3 billion in 2021 and is expected to grow at a compounded annual growth rate of 24.5% till 2030. Recent epidemic and containment strategies besides personalized medicine that expected to reduce the costs of unnecessary treatments, thereby improve outcomes.

Time series forecasting is conducted with quantifiable data. Retail stores use it to forecast sales, production, demand, and prices. It is also used to forecast inflation and credit scores. Transportation companies utilize time series forecasting to traffic. Financial institutions utilize it to forecast their revenues from mortgage payments. Healthcare industry use it to forecast the number of patients.

In the data sources where time is not a factor are named cross-sectional data. On the other hand, time series forecasting deals with time series data, which is collected through a specified time range. Time series data are collected on very frequent time scales such as stock market data at each tick; sales are recorded in real time; incoming patients also recorded in real time. For example, if the goal is to forecast next-day number of patients at a healthcare facility, using minute-by-minute patient data is likely to be less useful for forecasting than using daily or weekly aggregates. The minute-by-minute series will contain many sources of noise (e.g., variation by peak and non-peak). These errors, when the data are aggregated to an upper level, generally average out.

Prescriptive analytics

The information provided by prescriptive analytics can help determine the best course of action. We can gain insight on what course of action should be taken to reach optimal outcome. In other words, prescriptive analytics tells you how to react in the best way possible given the prediction.

Time series and regression-based forecasting is used in prescriptive analytics. Time series forecasting is conducted in quantifiable data. Time

series model has four components: level, trend, seasonality, and noise.

In order to assess the performance of the given model, it is tested on new data. Partitioning a time series into training and validation sets is the very first step. Methods are trained on first period, and their predictive performance assessed on the later validation period.

Many important problems involve many alternatives to effectively consider all of them at once. Prescriptive analytics utilizes optimization to identify the best solution to minimize or maximize the objective. The statistical and mathematical techniques can be coupled with optimization to make decisions that takes uncertainty into account.

Traditional data analysis techniques have often encountered challenges posed by big data applications such as scalability, high dimensionality, heterogeneous data. In common predictive analytics applications, data might come in text form, like physician records. For example, a physician might want to use an automated algorithm to classify patient visits as urgent or non-urgent, so that the urgent ones can receive immediate attention. The predictor features are embedded as text in documents.

A distinction should be noted between text processing for the purpose of extracting meaning and classifying. For the healthcare setting both techniques can be useful. The preprocessing steps that need to be done before text can be examined. The aim is to produce a matrix in which rows are terms and columns are documents. The nature of language include vocabulary reduction in the preprocessing step. The last step is to construct a quantitative matrix in which the metrics represent the occurrence, and the columns represent documents. Document labels (classes) are appended, and matrix is ready for labeled documents using classification methods.

Healthcare quality performance measures

There are growing trends in health departments that show serious commitment to increasing the successful implementation of quality improvement methods. The use of quality improvement will enable regional health departments to improve their performance and ability to protect, promote and maintain health in the communities they serve. Additionally, many public health departments are looking to quality improvement as a way to improve performance to meet accreditation standards. However, at present, there is little published evidence of the value and impact of quality improvement in public health, and only preliminary evidence is available on the factors that support the successful implementation and dissemination of quality improvement efforts in government health departments.

Quality improvement in healthcare might be applied to a wide spectrum of strategies and techniques. In this book chapter, we refer to

a quality improvement approach focusing on systems change to improve performance. Changes in outcomes can be assessed by data analysis which is listed before. This definition of quality improvement is based on the model for improvement.

The first step in improvement process is setting the aim. Then, defining the measures for the outcomes of interest which is very critical. Third step is to make changes from results of process analysis and root cause analysis. Final step is to test the effects of the changes on outcomes.

Planning stage includes identifying an aim, formulating an intervention, defining metrics, and putting a plan into action. Do (Execution) step includes the main component of the project. Study step involves monitoring outcomes to test the validity of the plan. Acting step closes the cycle, integrating the learning generated by the entire process and change methods, or even reformulate and improve.

This approach to quality improvement has been used to achieve improvements in public health infrastructure, policies, and the delivery of services. For example, health departments are currently applying PDSA to reduce costs, increase efficiency, increase customer satisfaction, create healthier environments in their community and improve health status outcomes of the populations they serve.

Main steps need to be followed can be listed as: 1) describe the target area for improvement that will be the focus of the quality improvement project; 2) describe the quality improvement methodology that will be utilized; 3) provide an outline of the evaluation plan and describes the specific focus of the evaluation.

Examples of quality improvement efforts include but are not limited to increasing the efficiency of public health services to lower costs, increase value of services, volume of people served, impact of services and customer satisfaction, implementing and assessing the effectiveness of evidence-based practices and approaches to improve the conditions that make people healthier, including prevention activities (e.g., immunizations, increased access to areas for physical activity, reduced exposure to environmental toxins); and/or improving health status indices for the populations served by the health department or reducing disparities in health outcomes between different populations in the community.

Potential areas for evaluation can be listed as costs and benefits of implementing; applicability for different types of targets like increasing capacity or improving health outcomes stakeholder satisfaction or enabling factors to the successful application of quality improvement in the healthcare facility.

To summarize, quality improvement is defined as a multidisciplinary, systems-oriented, data-driven method for understanding and improving the effectiveness, effectiveness and reliability of health processes and care outcomes. A quality improvement intervention is basically an effort to reduce the gap between the health care process and outcomes. The Centers for Disease Control department in the US has the use of health information technology for doctor or patient reminders; establishing standardized quality measures at the provider/system level for monitoring; doctor and patient education; to offer payment incentives to quality improvement practices for hypertension and cholesterol.

Compliance is a challenge in healthcare. Performance indicators need to be selected to monitor policy and systems changes. Proportion of health care systems with computer-based clinical decision support systems and the number of quality improvement initiatives to increase practitioner compliance can be listed.

Although process performance is measured, the existence of natural variation complicates the analysis, performance might not improve by subsequent runs. Traditional statistical analysis methods take into account of natural variation. They also require aggregation over time, in general this might delay decision making. Statistical techniques might yield insights into the data more quickly.

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