Generative Adversarial Networks in Healthcare Sector

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Abstract
Generative Adversarial Networks widely known as GANs, are deep learning models that has gained a lot of popularity in the last few years due to their promising nature. One of their major applications can be found in the healthcare sector for various purposes like image reconstruction, image enhancement, image segmentation, image processing, image analysis etc. The objective of this paper is to bring forward some of the recent research on the application of GANs in the health care domain during 2017 – 2022. A total of 168 papers were screened out of which 77 relevant to the present study were finalized for this study. Bibliometric analysis was also performed on these documents, to obtain an overall picture of Generative Adversarial Networks (GANs) in the healthcare domain. This analysis is expected to help the future researcher and developers in targeting the areas of the healthcare sector which are likely to grow in the coming future using GANs algorithms.

Keywords: Bibliometric Analysis; Deep Learning; Generative Adversarial Network; Healthcare

1. Introduction

Machine Learning (ML) is the capability of a machine to imitate intelligent human behaviour. ML algorithms are broadly divided into four types: supervised, unsupervised, semi-supervised and reinforcement learning. Today these algorithms are widely used in various fields such as social networking, virtual personal assistance, the banking sector, industry automation, self-driving cars, the healthcare industry, etc. Unsupervised learning algorithms mainly focus on understanding the relationships within a dataset. Among the unsupervised learning algorithms, Generative Adversarial Networks (GANs) have gained immense popularity these days in the healthcare domain [1]. Lan Goodfellow [2], introduced the concept of GANs in the field of deep learning models; These are a combination of adversarial neural networks in which gain to one network is a loss to another. Its architecture consists of two neural networks namely, a generator and a discriminator. The generator, through deep learning methods, learns and generates fake but credible image data, which is exactly similar to the real image data, whereas the discriminator's job is to scrutinize and differentiate between the original and fake data as shown in Figure 1. Image reconstruction, image enhancement, image segmentation, image processing, image analysis etc. are the major areas for the application of GANs [3]. This is particularly useful in case of deep learning models which depend heavily on the quantity and quality of data but many times it happens that sufficient amount of data is not available, due to which the model unknowingly learns the noise and deviations as well which leads to overfitting [4]. GANs models can produce synthetic data on which models can be applied to obtain results. It solves the data unavailability problem and reduces the risk of privacy concerns as plausible data is produced and used for analysis. They can also be used for text-to-image-generation, blurry images can be improvised, image-to-image translation, semantic image-to-text translation, 3D object generation and many more.

GAN have gained importance in the field of Telemedicine, remote monitoring, m-health (mobile health) and e-health (electronic health) system as they are capable of detecting any unusual situation [6]. Due to the combination of GAN algorithms along with IoT architectures have paved the way for telemedicine, e-health and m-health where it becomes convenient for both doctors and patients in understanding health condition. One of the major applications of GANs algorithm in the healthcare sector is in the area of medical imaging and diagnosis.

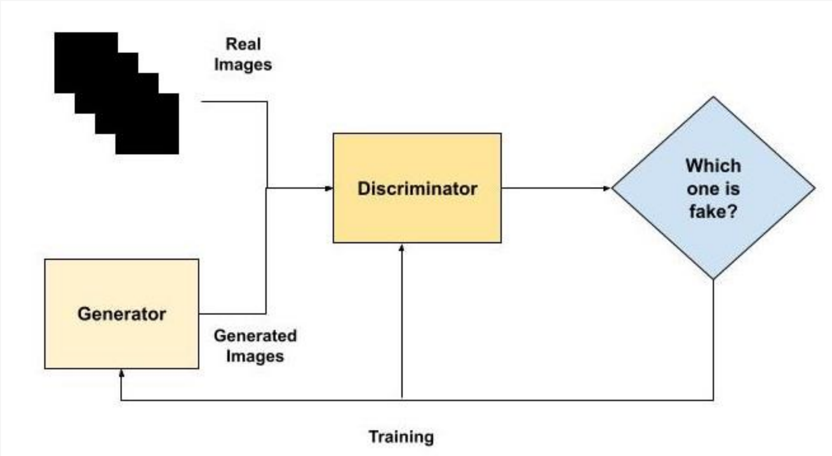

Figure 1: Working architecture of GAN [5]

The main objective of this paper is to bring forward the significance of GANs in the healthcare domain by analysing the earlier usage of this approach by researchers. To do so large volumes of scientific data have been analyzed and explored. To obtain relevant documents "Scopus" which has the largest dataset is considered. The present study tries to investigate the following which has the largest dataset is considered:

1) The major healthcare areas where GANs are employed.
2) Basic bibliometric analysis to highlight the growth and trend of GANs in the healthcare sector

The entire paper is divided into five sections: Section-1 provides an overall introduction and background of the study, followed by Section-2 mentioning the review papers related to GAN in different healthcare sectors. Section-3 of the study explains the working methodology and Section-4 provides information on the application of GAN in various domain of healthcare. Section-5 highlights the important findings and bibliometric analysis. Lastly, Section-6 provides conclusion and future scope of the study.

2. Background

To accomplish the objective of performing a Systematic Literature Review (SLR) on GANs in the healthcare sector various pieces of related works were studied as shown in Table 1. This helped in formulating research methodology by understanding methodologies employed by other researchers. Plethora of studies are available in the literature where the authors have performed a systematic review of the works available on the application of GANs in the healthcare domain. The paragraph below discusses some of the interesting reviews done by various authors from time to time.

In [7], the authors in their works of conducting an SLR on GANs and its application collected relevant documents from three libraries namely, Embase (Scopus), WoS (Web of Science), and PubMed. The analysis period from 2016 to 2020 was considered and a total of 2084 documents were retrieved followed by a two-phase screening was performed which helped in obtaining 52 potential documents for final analysis. The results obtained from the analysis mention that GANs had most of their application in the areas of medicine, diagnosis, 3-D object generation, Covid-19 pandemic, and image processing.

Following the standard procedure of an SLR in [8], the authors performed an analysis of the application of GANs for anomaly detection. Initially, documents from various digital libraries such as Science Direct, Scopus, ACM and IEEE Xplore were obtained. Then filtering was performed based on the title and abstract, followed by an ambiguity check and then lastly Cohen's kappa coefficient was calculated, and data were synthesized. Results revealed that the number of publications was progressively increasing from the year 2017 to 2020. The researchers [9], found that there was a significant growth in GANs in medical imaging in the year 2017-2018. This is because GANs can reduce the MR acquisition time by generating synthetic sequences. Considering another specific application of GANs in medical imaging, brain imaging, the authors performed an SLR. The relevant documents were chosen from PubMed using the keywords GAN, brain imaging, brain radiology and neuroradiology. The authors highlighted the fact that achievement of low-dose imaging through GANs while maintaining image quality or improving the image quality by removing artefacts by applying GANs can be of significant clinical relevance.

In [10], GANs technology can be employed for eye disorders and early detection of Glaucoma. They collected records from IEEE Xplore, Web of Science, Scopus, ScienceDirect, and PubMed databases for conducting SLR. The results obtained concluded that GANs are effectively used in image enhancement, reducing the computational time, and generating images for better classification to avoid class imbalance.

In [11], a literature review was performed on the overall applications of Generative Adversarial Networks. They considered review papers in the area of GAN architecture and variants, Computer vision, Image processing, medical imaging, speech processing, Deep fake, Video, Cyber security, Steganography and Finance. From their review, they concluded that GANs can train beyond the available data and requires limited human involvement and efficient generation of samples. Apart from image modelling GANs are also employed in the fields of time series forecasting and data imputation in the biomedical domain. To investigate GANs application in these areas conducted an SLR. A total of 1057 relevant records were obtained from their digital databases namely Scopus, Web of Science and PubMed. Ultimately 99 records were finalized, and analyses were performed on them. The authors concluded that apart from Image data, GANs can also be applied in forecasting non-visual time series data. Image segmentation is one of the challenging jobs in the healthcare domain.

In [12], the authors conducted a literature review considering the application of GANs in medical image segmentation. Google Scholar and PubMed were used for document collection. The authors categorized the papers based on segmentation regions, imaging modality, and classification methods. The researchers concluded that GANs have good generating and capturing data distribution abilities which increase the accuracy of image segmentation.

In [13], the authors performed an SLR on creating artificial images for radiology using GANs. PRISMA guidelines were followed and documents during 2017-2019 were chosen for selection. The authors revealed that GANs have major applications in the area of image reconstruction, image segmentation, scan time reduction, and data augmentation for radiology. The authors considered ELSEVIER, IEEE Xplore, and Springer and obtained 105 related papers. They mainly investigated the subject of medical image augmentation in which a review of the relationship between augmented models and training sets was considered, a summary of various evaluation metrics, and the advantages of augmented models were highlights of the research.

In reference [14], the authors performed an SLR of GANs architecture in medical image segmentation and classification. PRISMA guidelines were followed, and 54 papers were finalized. The period of analysis was from 2015 to 2020. The authors concluded that four GANs architectures were widely employed in medical image segmentation and provided an overview of GANs applications. Mentioning GANs in biomedical image segmentation [15], investigated various GANs architectures. They conducted an SLR, followed by a two-screen folding and finalized 138 relevant articles. Their study revealed that vanilla GAN and conditional GAN architecture were used in biomedical image segmentation. They also provided an overview of GANs application in various human diseases. In [16], the authors investigated the role of GANs in addressing covid-19 challenges. An SLR was performed by collecting PubMed, IEEE Xplore, Association for Computing Machinery (ACM) Digital Library, Scopus, and Google Scholar documents. The results concluded that data augmentation using GANs improved the performance of AI techniques such as CNN.

In addition, GANs were used for the evaluation of chest X-ray and CT scan images. In [17], the researchers worked on exploring emerging implementation trends and limitations of GANs in tumour-related problems and conducted an SLR. After a screening of the documents 35 related documents were used for analysis. They found that most of the research was conducted in the area of the brain, followed by the lungs and breasts. Mostly GANs were employed for tumour segmentation followed by tumour detection and classification. [18] and [19] mentions the application of GAN in the areas of medical deep learning and computer vision.

3. Methodology

This section deals with the procedure and methodology opted for conducting an SLR on GANs and their application in the healthcare sector. SLR helps in answering a specific framed question by intensifying, assessing and critically appraising research. It helps in identifying the research gaps in the field and provides a comprehensive overview of a particular topic. This helps future researchers in gaining an overall insight and then find the appropriate direction to conduct research in a specific field. The entire methodology is divided into five stages namely,

1. Formulating the research question(s)
2. Identifying keywords to be analyzed
3. Assessing the obtained documents
4. Thoroughly analyzing, discussing, and identifying the future scope

Table 1: Highlights reviews done in the area of the application of GANs in the healthcare domain

References	Reference number	Field of study	Number of documents	Period of Analysis
Chen et al., 2022	[1]	Medical Image augmentation	105	2013-2018
Laino et al., 2022	[3]	Brain Imaging	46	2018-2021
Festag et al., 2022	[4]	Biomedical time series forecasting	33	2014-2022
Asimopoulos et al., 2022	[7]	Identification of major ideas of research including healthcare and different GAN architectures employed.	59	2018-2021
Sabuhi et al., 2021	[8]	Applications of GAN in Anomaly Detection	128	2017-2020
Yi et al., 2019	[9]	Medical imaging	150	2017-2018
Saeed et al., 2021	[10]	Glaucoma detection	59	2015-2020
Aggarwal et al., 2021	[11]	Analysis of recent GAN models in areas application and challenges including healthcare	52	2016-2020
Xun et al., 2021	[12]	Medical image segmentation	120	Till September 2021
Sorin et al., 2021	[13]	Creating artificial images for radiology applications	33	2017-2019
Jeong et al., 2022	[14]	Medical image classification and segmentation	54	2015-2020
Iqbal et al., 2022	[15]	Biomedical image segmentation	138	2016-2021
Ali and Shah, 2022	[16]	Combating Covid-19 using GAN and AI for medical images.	57	2020-2022
Behrens et al., 2022	[17]	Tumor-related research	35	2014-2021
Egger et al., 2022	[18]	Medical deep learning	40	2017-2020
Park et al., 2021	[19]	Computer vision	111	2014-2020
This paper	---	GAN in healthcare sector	77	2017-2022

Table 2: PRISMA rules and results obtained from the Scopus

Review protocol elements	Authors' consideration	Results in terms of sources
What is already known? and Research topics	Generative Adversarial Network (GAN) has become a buzzword in the market from already known knowledge; it has got many applications including healthcare management. Due to its popularity and significant growth, there is the potential for a structured literature review (SLR) investigating how GANs can contribute to healthcare management.	168
Journals' and thematic limitations	The journals related to various fields namely medicine, biochemistry, neuroscience, health professions, genetics, decision science, Toxicology Pharmaceutics and many more were considered. Thus the study provides a broader picture of GANs applications in various healthcare sectors rather than confining to a particular disease or a particular field.	81
Other restrictive elements Period of analysis	The authors selected only open-access documents written in English. 2017 to till November, 2022	77

A structured methodology adhering to PRISMA rules as shown in Table 2 is followed where firstly a research question is framed. Once the question is formulated keywords that are relevant to it are selected. Using the selected keywords, a search is performed in the Scopus digital library. As shown in Table 2 Analysis period from 2017 to November 2022 is chosen. The documents obtained are thoroughly assessed and the most appropriate one is chosen for analysis purposes. Bibliometric analysis is performed and an overall overview of the topic is obtained with the help of various charts and graphs. Figure 2 below depicts the methodology which broadly comprises four sections, namely,

1) Identification 2) Screening 3) Eligibility, and 4) Analysis. The proposed methodology helps in obtaining relevant document, which would be further used in performing bibliometric analysis. Figure 2 depicts the proposed methodology for the study.

Step-1 Identification: This is the very first step in performing a Systematic Literature Review, where based on the research question formulated, relevant keywords are chosen. “Generative Adversarial Networks” and “Healthcare” were the most promising keywords found. The keywords obtained were used to figure out the relevant documents. “Scopus” database was used to find out documents.

Step-2 Screening: This step of SLR is considered a data reduction step. An analysis period of six years was considered starting from 2017 to Nov 2022. This is because as per the related works (Section-2) GANs have gained popularity from the year 2017. About 168 documents were obtained after checking for duplications. Further, screening was performed, and 87 documents were excluded and only 81 documents were included as they were open source.

Step-3 Eligibility: The relevant documents obtained from the previous step were checked by eligibility to confirm their relevance to the raised question. The following filters were applied.

- Only the Open Access documents were selected for review purposes.
- Article, Conference and Review papers were considered.

Finally, a total of 77 documents were obtained and these were used for conducting bibliometric analysis.

Step-4 Analysis: In the final step of the methodology “Bibliometric analyses” were performed on the selected 77 documents obtained from step-3. The study concentrates on gaining insights on

1. Overview of GANS in healthcare
2. Keyword analysis
3. Source analysis

Performing the above-mentioned analysis will help to obtain an overall picture of GANs in healthcare. In addition, answers to many questions can be obtained such as what are the most fields in which GANs are applied, and which journal has got the greater number of citations in this particular field of study.

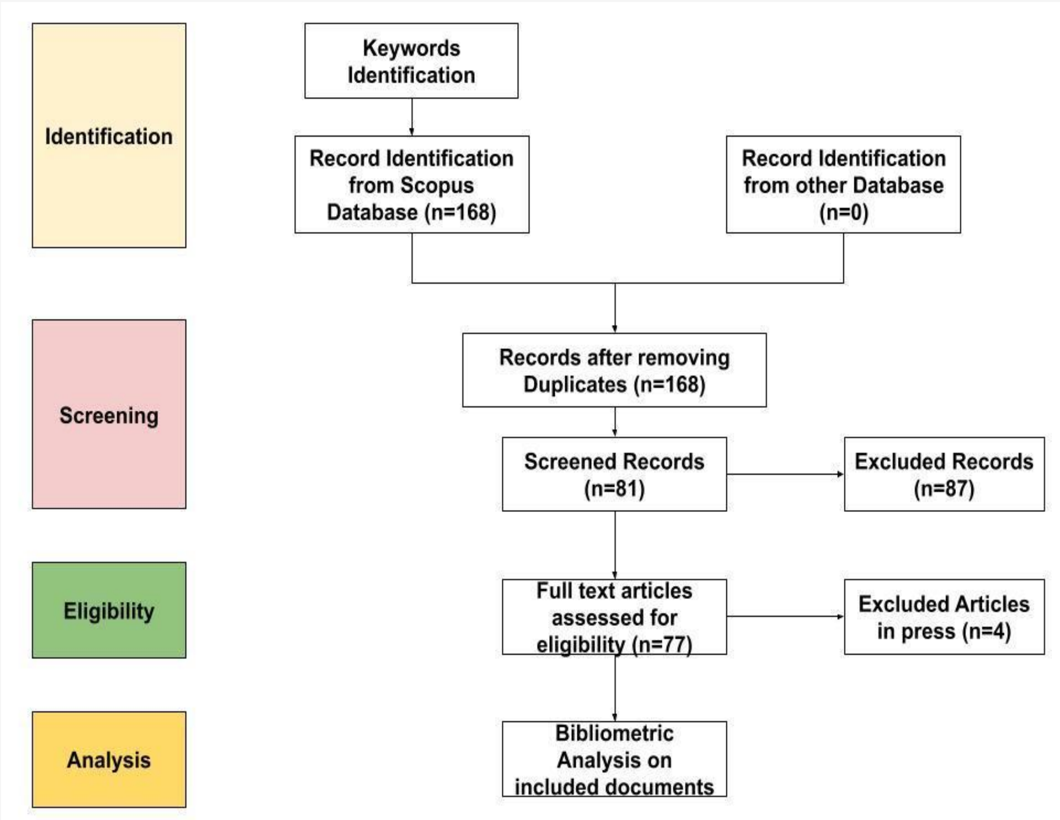

Figure 2: Methodology workflow

4. Application of GAN in Various Domain of Healthcare

4.1 Medicine

The world is moving towards automated medicine, this concept has uplifted the importance of ultrasound, and images in predicting and diagnosing a disease in reference [20]. Due to the unavailability of enough images, it is difficult for programmers to train, build and run deep-learning models on a dataset. GANs can generate synthetic images which are very similar to real images was observed [21] and can be used for data analysis. Various GAN versions were employed by different authors, DGGAN (Deep Convolutional Generative Adversarial Network) is the most widely used algorithm for synthetic data generation. Using GANs synthetic images for complicated datasets of lung cancer [22], PPG (Photoplethysmogram) [23], medical data [24], CT and MRI images [25] and Chronic Obstructive Pulmonary Disease (COPD) [26] were generated. Apart from these [27], the authors mention that CGAN (Cycle consistent GAN) was employed to normalize the MRI (magnetic resonance imaging) images for breast cancer. [28] mentions that Convolutional GAN is employed for private medical data generation. The authors in [29] proposed a unique model FedGAN (federated GAN) for medical image generation. In addition, the Bank of GAN was used [30] for the effective transmission of medical images. The application of GAN's in the medicine domain is shown in Table 3.

4.2 Image Processing

One of the important applications of GANs is in the area of image processing which includes image reconstruction, image enhancement, 3D image generation, image improvisation and image segmentation as shown in Table 4. In [31] and [32], the authors employed DR-LL Gan and GAN for improvising Diabetes retinopathy and CT scan images respectively and for improvement of stomach cancer CT images the authors in [33]. Whereas Semi-supervised GAN was employed for CT image feature extraction and generation in [33]. Multi-stage feature extraction GAN(MF-GAN) are effective in denoising the CT images and 3D reconstruction of image texture and edges was found by the authors in [34]. Image segmentation in the case of a sensitive and complex organ such as the brain is a challenging job. In [35], the authors concluded that Multistage GAN can be effectively used for medical brain image segmentation. Progressively Growing Generative Adversarial Network a version of GAN was employed by the authors for image generation and manipulation in reference [36]. Highlighting the application of Conditional GAN in image processing the authors in [37-39] mentions that CGAN are used for image reconstruction, segmentation and image enhancement. Enhanced super-resolution GAN was used by authors in [40] for image quality enhancement for skin cancer.

Table 3: Application of GAN in medicine

Authors	Reference number	Year	Model	Application
Arvanitis T. N. et al.	[20]	2022	GAN	To generate realistic synthetic datasets
Torfi et al.	[28]	2022	Convolutional GAN	Synthetic private medical data generation
Jin et al.	[29]	2022	federated GAN (FedGAN)	Medical image generation
Chang C. et al.	[30]	2021	Bank of GAN	Effective transmission of medical images
Gonzalez et al.	[22]	2021	GAN	To generate synthetic data for lung cancer treatment.
Kumar et al.	[21]	2021	DCGAN	To generate synthetic ultrasound images.
Modanwal et al.	[27]	2021	Cycle consistent GAN	To normalize MRI images for breast cancer.
Shin H. et al.	[23]	2021	GAN	Generate synthetic PPG (Photoplethysmogram) data
Vaccari et al.	[26]	2021	GAN	To generate synthetic data for Chronic Obstructive Pulmonary Disease (COPD) monitoring
Thambawita et al.	[24]	2021	Deep GAN	Synthetic medical data generation
Bourbonne et al.	[25]	2021	2D-GAN	Synthetic data generation for CT and MRI images

Table 4: Application of GAN in image processing

Authors	Reference number	Year	Model	Application
Abbood et al.	[31]	2022	DR-LL GAN	Image enhancement for diabetes retinopathy images
Deshmukh and Bhat	[36]	2022	Progressively Growing Generative Adversarial Network	Image generation and manipulation.
Khaled et al.	[35]	2022	Multi-stage GAN	Segmentation of brain medical image
La Salvia et al.	[6]	2022	DCGAN	To generate synthetic hyperspectral images for skin cancer diagnosis
Alwakid et al.	[40]	2022	ESRGAN	Image quality enhancement for skin cancer using Enhanced super-resolution generative adversarial networks
Lupion et al.	[37]	2022	CGAN (Conditional GAN)	Image reconstruction
Chopra et al.		2022	Cyclic GAN	Image quality enhancement for breast cancer images
Pawar et al.	[38]	2022	CGAN (Conditional GAN)	Image segmentation for lung disease classification
Zhang et al.	[34]	2021	Multi-stage feature extraction GAN(MF-GAN)	Denoising the CT images and 3D reconstruction of image texture and edges.
Oluwasanmi et al.	[33]	2021	Semisupervised GAN	CT images feature extraction and image generation
Ghani et al.	[39]	2019	CGAN (Conditional GAN)	Image enhancement of CT scan images
Sharma et al.	[32]	2019	GAN	To improvise CT scan images of stomach cancer

4.3 Data Augmentation

In reference [41] [42] [43] and [44] SynSigGAN and time series to time series GAN are employed for synthetic medical data generation and for fake ECG, EHR, EMG, EEG and PPG data generation. Electronic health records (EHR) are difficult to find due to security concerns and mostly if found most of them are imbalanced datasets. Another widely used application of GAN is data augmentation. It is mainly used to balance the datasets in terms of the output labels. In [45], the authors developed a version of GAN namely ehrGAN which was used for synthetic data generation for EHR. Similarly, in [46], the authors employed GAN for realistic EHR generation. Conditional GAN was employed by [47] for data augmentation of infrared sensors. In [48], the authors employed a novel model of pixel-to-pixel GAN for medical synthetic data augmentation. The application of GAN's in the data augmentation domain is shown in Table 5.

4.4 Decision Making

In addition to various applications in medicine, data augmentation, image processing etc. GAN are also used in the area of decision making as shown in Table 6. Detection of disease organisms for complex diseases is a difficult job. In [49], the authors in their research found that CGAN is effective in detecting Mycobacterium tuberculosis (Mtb) organisms. DCGANs are best for detecting task difficulty for learners in colonoscopy as found by the authors [50]. Neural-Symbolic Learning [51] was used along with GAN for the detection and generation of spinal structure reports. In reference [52] and [53] the authors in their research on anomaly detection found that Deep GAN and PGGAN are effective.

4.5 Covid-19

It is seen that GANs have gained popularity in the healthcare sector from the year 2019. This was also the year where covid-19 pandemic started. Whereas DCGAN was used [54] in speech signal processing for Covid-19 detection. In [55], the authors in their research on covid-19 detection using CT scan images employed DCGAN to generate a synthetic version of CT scan images. Whereas in [56], the authors in their work considered Semi GAN (SGAN) for the removal of unequal class densities in covid data. In [57] [58] used Cyclic GAN for image segmentation and data augmentation of covid-19 dataset. In [59] the authors proposed a Randomize GAN for image detection for unknown classes. The application of GAN's in the Covid-19 domain is shown in Table 7.

4.6 Miscellaneous

Apart from synthetic data generation GANs have been employed by researchers in various other data processing fields shown in Table 8. In [60], the authors used GAN-AD for anomaly detection whereas, in [61], the researchers employed SIG-GAN for filling in the missing data for missing sequences of EEG signals.

Table 5: Application of GAN in data augmentation

Authors	Reference number	Year	Model	Application
Arumugasamy et al.	[47]	2022	CGAN (Conditional GAN)	Data augmentation of infra-red array sensors
Aljohani et al.	[48]	2022	Deep Pix2Pix GAN	Synthetic medical image generation
Alosaimi et al.	[77]	2022	GAN	Comparative study of GAN and CNN for data augmentation
Brophy et al.	[42]	2021	time-series-to-time-series GAN	Generation of high-quality PPG signal.
Potekhin et al.	[43]	2021	GAN	Synthetic data generation for EEG data
Piacentino et al.	[44]	2021	GAN	Generating synthetic ECG medical data
Hazra et al.	[41]	2020	SynSigGAN	Synthetic generation of biomedical images (ECG, EMG, EEG and PPG)
Lee S. H.	[46]	2018	GAN	To generate fully synthetic EHR
Che Z. et al.	[44]	2017	ehrGAN	Data augmentation for EHR

Table 6: Application of GAN in decision making

Authors	Reference number	Year	Model	Application
Zachariou et al.	[49]	2022	Cycle GAN (CGAN)	Detect Mycobacterium tuberculosis (Mtb) organisms
Balaji et al.	[52]	2022	Deep GAN	Detecting malicious intruders
Liu X. et al.	[50]	2021	DCGAN	To detect task difficulty for learners in colonoscopy
Kwon et al.	[53]	2021	PGGAN	Anomaly detection for chest X-ray images
Han Z. et al.	[51]	2020	GAN and Neural-Symbolic Learning	To detect and generate a report on spinal structures

Table 7: Application of GAN in Covid-19

Authors	Reference number	Year	Model	Application
Serte et al.	[55]	2022	DCGAN	Generate a synthetic version of a CT scan for Covid-19 detection
Tavakolian et al.	[56]	2022	SGAN (Semi GAN)	Removal of unequal class densities in covid data
Connell et al.	[57]	2022	CGAN (Cyclic GAN)	Image segmentation of Covid-19 scans
Al-Dhlan A.K et al.	[54]	2022	DCGAN	Speech signal processing for Covid-19 detection,
Motamed et al.	[59]	2021	Randomize GAN (RANDGAN)	Image detection for unknown classes in Covid-19 data
Hernandez et al.	[58]	2021	CGAN (Cyclic GAN)	Data augmentation for the Covid-19 dataset

It was seen by the authors in [62] that electrocardiogram signals used for heart monitoring can be improved through DCGAN. CGAN and improved fuzzy c-means clustering (IFCM) were used [63] for detecting multi-class voice disorder. In [64], the authors used IoT along with DCGAN to monitor maternal and fetal health status. The authors mentioned that Variance GAN (VGAN) were successful in predicting medical expenditure in reference [65]. GAN is employed with other disciplines for improving the quality of annotated data [66] and [67] the authors employed deep ensemble learning model with GAN for improving the quality of annotated data. Reference [68] and [69] found that GAN can also be applied to time series data. Whereas in [70] employed pix2pixGAN for improving signal-to-noise ratio for CT images. In [71], employed GAN with a whale optimization algorithm to improve the feature extraction. In [72], GAN was used for the detection of organ ageing. Apart from these, the authors choose GAN for synthetic data generation in the case of Alzheimer's disease in [73]. GAN can also be used in patient monitoring [74] and recommendation of next-day activities [75], maximizing sensors information [76] and for classification of oral squamous cell carcinoma conditions [77]. Synthetic data can address data scarcity, fostering progress in medical research and innovation.

Table 8: Application of GAN in Miscellaneous domains

Authors	Reference number	Year	Model	Application
Anbarasu et al.	[66]	2022	Deep ensemble learning model (DELM) + GAN	Improving the quality of annotated data and solving unbalanced annotated data
Park et al.	[67]	2022	Fast unsupervised Anomaly detection + GAN (F-AnoGAN)	Improving anomaly detection in the chromate process
Zheng et al.		2022	PPG GAN	To remove noise from the PPG (Photoplethysmography) signals
Venkatasubramanian	[64]	2022	DCGAN and IOT sensors	To monitor high-risk maternal and fetal health
Gatta et al.	[68]	2022	GAN	Time series analysis
Riaz et al.	[71]	2022	GAN+ Whale Optimization Algorithm	For feature extraction of Covid-19 images
Saeed et al.	[74]	2022	GAN	Patient monitoring using wireless technology
Li et al.	[75]	2022	GAN	Recommendation system for next day medical activity
Ajay et al.	[76]	2022	INFOGAN	Maximizing information collected from sensors during physical exercise.
Alosaimi et al.	[77]	2022	GAN	For classification of oral squamous cell carcinoma condition
Lee et al.	[61]	2021	SIG-GAN for signal sequences	To generate missing data for missing sequences of EEG signals.
Logan et al.	[73]	2021	DCGAN	Synthetic data for a Alzheimer's disease
Chui k. et al.	[63]	2020	CGAN and improved fuzzy c-means clustering (IFCM)	To detect multiclass voice disorder
He Y. et al.	[62]	2020	DCGAN	Enhance the ECG (electrocardiogram) signals that monitor heart signals.
Hao et al.	[70]	2020	pix2pixGAN (Pixel to Pixel GAN)	Improving signal-to-noise ratio of optical coherence tomography images
Dash et al.	[69]	2020	GAN	Generation of synthetic medical time series data.
Kaushik et al.	[65]	2020	Variance based GAN (V-GAN)	To predict medicine expenditure
Naidoo K.	[60]	2020	GANs anomaly detection (GAN-AD)	Anomaly detection
Zhavoronkov et al.	[72]	2019	GAN	For detection of ageing of organs

By using GANs to create synthetic data, patient privacy can be preserved by avoiding direct personal identifiers, though there is a risk of retaining identifiable patterns. Therefore, it is crucial to ensure that the creation and use of synthetic data comply with regulations such as HIPAA in the US, GDPR in Europe, and other relevant privacy laws. Additionally, efforts should focus on mitigating biases in synthetic data generation to promote fair and equitable healthcare research and applications. Furthermore, continuous monitoring of synthetic data's impact on healthcare outcomes is essential to identify and resolve any ethical issues that may arise.

5. Results

After obtaining relevant records from the Scopus Database, Bibliometric analysis was performed to gain insights into them. R studio 'Bibliometrix package' was used for performing analysis. Bibliometrix is an R software package that provides all the instruments to perform bibliometric analysis. A simple bibliometric analysis was performed in which overall important statistics were stated. Followed by analysis namely; annual scientific production showcasing the growth, word cloud revealing the prominent keywords of the GANs area, and lastly, leading journals in this area were found. As shown in Figure 3, a total of 77 documents were finalized out of which 68% were articles, 20% were conference papers and 12% were review papers. The timespan considered was from the year 2017 to November 2022. A Pie chart of number of applications of GAN is provided in Figure 4.

5.1 Annual Scientific Production

The bar graph in Figure 5 reveals the annual scientific production is steadily increasing from the year 2017 to November 2022.

5.2 Word Cloud

The below figure depicts the most frequent keywords used in the documents by the authors. The size of the keyword is directly proportional to the number of times a keyword is used. The larger the size, the more frequent a keyword is. From the Figure 6, it can be seen that keywords namely deep learning, machine learning, deep convolutional generative adversarial network (DCGAN), data augmentation, medical imaging, anomaly detection, cycle GAN (CGAN), synthetic data generation, medical image analysis, healthcare etc. were the most prominent words.

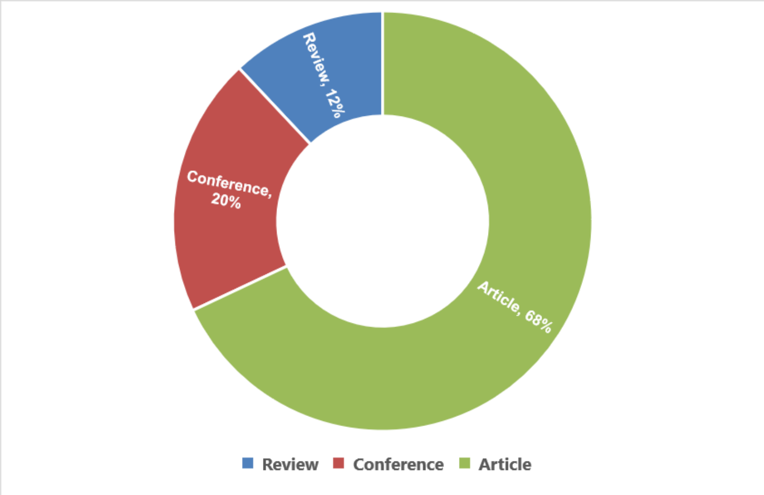

Figure 3: Percentage usage of GAN in different reviewed applications areas

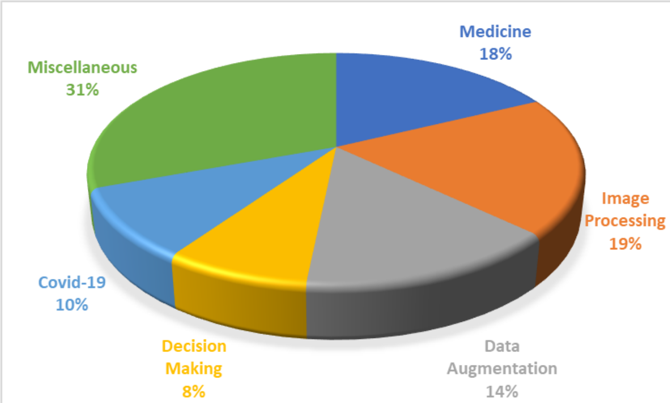

Figure 4: Percentage usage of GAN in different reviewed applications areas

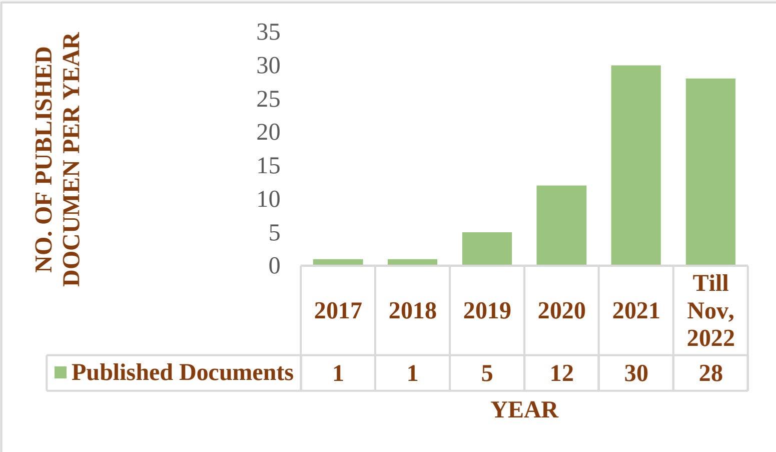

Figure 5: Annual Scientific Production per year

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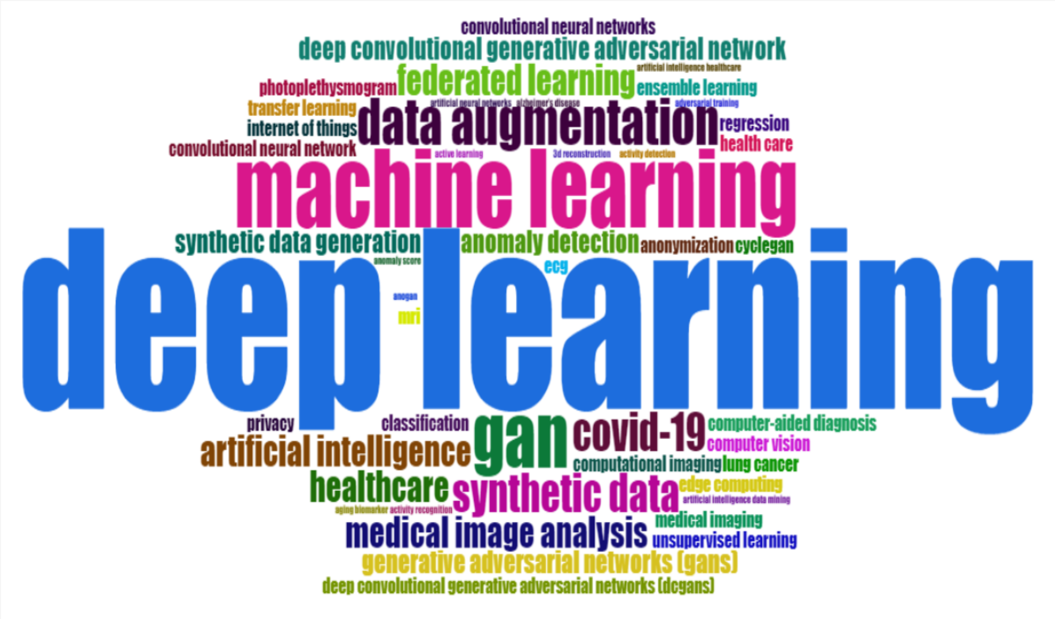

Figure 6: Word cloud

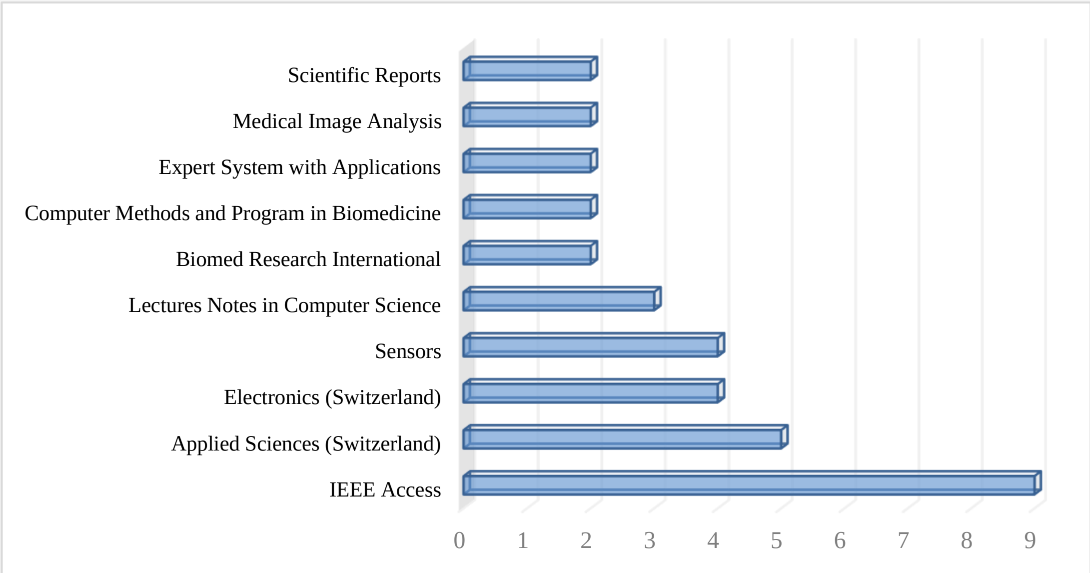

Figure 7: List of top ten sources among 52 sources

5.3 Most Relevant Sources

From the analysis, as shown in Figure 7, it was found that there are 52 sources were related to our collection, out of which the top ten sources with the highest number of documents related to GAN in healthcare are depicted below. For the publication of an article or to get good information about a subject, it is important to know the top journals in that area. The above bar chart represents the top ten most relevant sources of GANs among the 52 sources along with the number of documents published in the healthcare sector. It is depicted that 'IEEE ACCESS' is the most relevant journal in this area. Whereas Applied Science (Switzerland), and Electronics (Switzerland) journals also have relevant articles to the study.

Important Findings:

1. Medical Image analysis, Data augmentation, Synthetic data generation, and disease detection were found to be trendy topics in which GANs are widely employed.
2. From the application point of view, it can be seen that GAN has been applied to various fields however, image processing, medicine, and data augmentation are the three areas where GAN has

been used the most frequently, accounting for 19%, 18%, and 14% of the total number of papers taken into consideration in the paper.

3. Overall annual scientific production section reveals that the application of GAN in the healthcare sector is growing annually at a significant rate of 94.73%
4. GAN implementation in various domains of healthcare:
   a. From the literature review developed it is seen that Deep Convolutional GAN (DCGANs) in healthcare is the most widely used GAN architecture. It is being employed in various fields such as the generation of synthetic data, enhancement of inputs and disease detection.
   b. Cyclic GAN widely known as CGAN is observed to be one of the most important types of GAN architecture in disease decision-making and image normalization.
   c. Some other architectures of GAN: It can also be noted that in addition to other GAN architectures VGAN (prediction), Multi-Stage (image reconstruction and segmentation) GAN, Semi-GAN (removal of class densities) various other versions of GAN namely ehrGA, improved fuzzy c-means (CGAN & IFCM) are used in data augmentation, pre-processing and detection.
5. Hybrid model of GANs: It is seen that GAN is also used in combination with IOT sensors for disease prediction, and symbolic learning for image synthesis and generation showcasing its hybrid ability.
6. From the analysis IEEE access, electronics (Switzerland), and Applied science (Switzerland) were the top three leading journals for publishing articles in this field.

6. Conclusion

Overall annual scientific production section reveals that the application of GAN in the healthcare sector is growing at a significant rate. Performing Bibliometric analysis has helped in finding unexplored areas, understanding the trend of scientific publication, and categorization topics based on emerging, trending, and basic. The research helps in gaining a complete overview of the implementation of various GAN algorithms and techniques in healthcare institutions. Apart from the analysis, the literature review and analysis helped in understanding various applications of GAN in healthcare institutions such as the use of image enhancement, medical image analysis, classification, data augmentation, synthetic data generation, federal learning etc.

This analysis would help the future researcher and developers in targeting the areas of the healthcare sector which are likely to grow in the coming future using GAN algorithms. Problems with the GAN model are Generator loss can lead to GAN instability which is unaddressed. Comparison of the quality of images generated through various GAN models can be compared. Another difficulty with GAN is that they need a lot of data to train, therefore changing the GAN architecture can address this problem. It is possible to compare which GAN version performs image filling the best. As GANs are widely known for synthetic image generation but at times they generate redundant images, thus medical image compression technique must be employed to improve the cost-effectiveness.

7. Future Scope

From the above-mentioned, Literature review though it is evident that GAN has gained popularity in various areas of the healthcare sector there are a few areas where a little amount of work is being done such as the application of GAN in pre-processing which includes enhancing ECG, generating missing data, removal of class biases, detection of voice disorder, normalizing of images. A very small amount of work is done in the area of anomaly detection using GAN which is considered to be one of the prominent steps in deep learning. Further research can be conducted on addressing the GANs problem of diminished gradient (the discriminator gets too successful that the generator gradient vanishes and learns nothing) and mode collapse (the generator collapses which produces limited varieties of samples).

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