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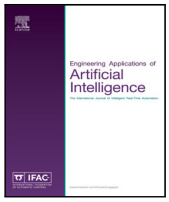

Survey paper

Ovarian cancer data analysis using deep learning: A systematic review

Muta Tah Hira [a,1], Mohammad A. Razzaque [b,1,*], Mosharraf Sarker [c]

[a] School of Health and Life Sciences, Teesside University, UK
[b] School of Computing, Engineering and Digital Technologies, Teesside University, UK
[c] Pharmacy and Biomolecular Sciences, Faculty of Science, Liverpool John Moores University, UK

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ABSTRACT

Technological advancement and the adoption of digital technologies in cancer care and research have generated big data. These diverse and multimodal data contain valuable high-density information on various cancer subdomains, including early detection and accurate diagnosis. By extracting this information, machine learning or deep learning (ML or DL)-based autonomous data analysis tools can help clinicians and cancer researchers discover patterns and relationships from complex datasets. Many DL-based analyses on ovarian cancer (OC) data have recently been published. These analyses are highly diverse in various aspects or features of cancer (e.g., subdomain(s) and cancer type they address) and data analysis features (e.g., data modality, analysis method). However, a comprehensive understanding of these analyses in terms of these features and Artificial Intelligence Assurance (AIA) is currently lacking. This systematic review aims to fill this gap by examining the existing literature and identifying important aspects of OC data analysis using DL, explicitly focusing on key features and AI assurance perspectives. We used the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework for detailed searches across three journal databases and included only peer-reviewed studies published from 2015 to 2023. We identified and reviewed 96 DL-based OC studies and found five important insights on DL-based OC data analysis. First, most studies 71% (68 of 96) focused on detection and diagnosis, while no study addressed the prediction and prevention of OC. Second, the analyses were predominantly based on samples from a non-diverse population (75% (72/96 studies)), limited to a geographic location or country. Third, only a small proportion of the studies (only 33% (32/96)) performed integrated analyses, most of which used homogeneous data (clinical or omics). Fourth, only 8.3% (8/96) of the studies validated their models using external and diverse datasets, highlighting the need for enhanced model validation, and finally, the inclusion of AIA in cancer data analysis is in a very early stage; only 5.2% (5/96) explicitly addressed AIA through explainability. We also highlight critical areas that require attention in DL-based cancer data analysis, especially OC data analysis. Future research should address identified gaps, including exploring diverse and heterogeneous integrated data-driven analyses, validating models using external datasets from different demographic populations, and focusing on AI assurance through all aspects, including explainability and safety.

1. Introduction

Ovarian cancer (OC) is a widespread and fatal gynaecological cancer with a high death rate in developed countries. It causes 5% of all cancer deaths in women in the UK (UK, 2020) and the USA (Torre et al., 2018). OC is often diagnosed at an advanced stage due to its asymptomatic early stage and nonspecific symptoms at a later stage (Doubeni et al., 2016). Furthermore, the location and position of the ovaries make it difficult to detect until the ovarian mass is large or metastasis occurs. Early detection and diagnosis of OC are difficult due to its nonspecific symptoms, and multiple doctor visits and tests may be required. In this context, advanced technology-driven research on the underlying mechanisms of cancer can lead to better diagnostic tools, better treatments, and a more accurate prognosis (Doubeni et al., 2016; Lu and Zhan, 2018).

Rapid development of technology, such as high-throughput technologies and information communication technology (ICT), has resulted in the generation of a large amount of data in cancer research and care. These big data mainly include clinical data such as various modalities of image data (e.g., Magnetic Resonance Imaging (MRI), histopathological), molecular or multi-omics (Zhang et al.,

* Corresponding author.
E-mail addresses: m.hira@tees.ac.uk (M.T. Hira), m.razzaque@tees.ac.uk (M.A. Razzaque), m.h.sarker@ljmu.ac.uk (M. Sarker).
[1] First and second authors contributed equally.

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2019b; Chen et al., 2022; Saida et al., 2022; Hira et al., 2021), and cancer management-related data (e.g., personal management data De Silva et al., 2018a). These data, especially histopathological images and molecular data, contain high-density information, such as predictive and prognostic molecular biomarkers, which are helpful in early detection and accurate cancer diagnosis. Extracting this information requires autonomous data analysis tools such as AI/ML/DL as they are impossible to extract by human experts (e.g., radiologists and pathologists) (Echle et al., 2021). As a result, the ML and DL approaches (Echle et al., 2021; Zhang et al., 2019b; Hira et al., 2021) have become valuable tools in cancer research and care. These approaches allow researchers to analyse large and complex datasets, leading to discoveries and insights that can improve diagnosis, treatment, and prognosis. In the past decade, more than 50 thousand research works (searched on Google and other databases) have been published on ML for cancer, and many of them are in OC (Hira et al., 2021; Zhang et al., 2019a; Zhao et al., 2020; Wang et al., 2022b; Han et al., 2022; Kim et al., 2021; Zhu et al., 2021). Many of these works are based on DL, as the Artificial Neural Network (ANN) of DL allows the models to handle increasing amounts and diversity of data efficiently (LeCun et al., 2015). This efficiency makes DL particularly effective in tackling complex computational issues, such as large-scale image classification and integrated multi-omics analysis of cancer (LeCun et al., 2015).

Although DL-based data analyses, such as cancer diagnosis and treatment selection, offer significant benefits, they also introduce risks that must be addressed. The autonomous, complex and scalable nature of DL/ML systems presents risks that extend beyond those posed by typical software. These characteristics fundamentally challenge our current methods for evaluating and mitigating the risks associated with digital technologies (Mökander et al., 2021), including DL-based cancer analyses. To ensure effective and wide-scale adoption of AI systems in any domain, including cancer (Hasani et al., 2022), they must ensure that they function as intended. To offer such assurance, it is necessary to quantify capabilities and risks in various dimensions, including data quality, algorithm performance, statistical considerations, trustworthiness, security, and explainability. Furthermore, assurances in many dimensions must be domain-specific (e.g., cancer) as a generic assurance solution in all subareas and domains could be suboptimal (Batarseh et al., 2021). For example, a DL system segmenting kidney images as an initial task for radiologist evaluation requires a different level of trust than a DL system diagnosing cancer and initiating chemotherapy.

The articles published on any individual cancer, such as OC, are highly diverse, mainly in terms of (i) type of cancer (e.g., high-grade ovarian serous carcinoma (HGOSC), low-grade serous ovarian carcinoma (LGSOC)) they address, (ii) their aims or goals (e.g., prediction, detection, diagnosis), (iii) types (e.g., image, molecular) and origin or source (e.g., cell, tissue) of the data, (iv) data integration methods used for the analyses and their ML/DL approaches (e.g., CNN- Convolutional neural network, LSTM- Long Short-term memory). For example, Zhang et al. (2019a) used a fine-tuned GoogLeNet (Szegedy et al., 2014) – a deep CNN architecture – to extract high-level features from OC ultrasound (US) images for further analysis. On the other hand, Hwangbo et al. (2021) developed ML and DL models to predict platinum sensitivity in patients with HGSOC. Considering the importance of OC data analysis in risk prediction, early detection, and accurate diagnosis and prognosis, a holistic view of these diverse DL-based analyses, including the AIA perspective of these analyses, is essential. However, no work provides a holistic view of the field. Therefore, this study provides a holistic view of the field through a systematic review of DL-based OC data analyses from key features and AIA perspectives. This review will try to answer the following research questions:

1. What are the key features of an ML/DL-based cancer data analysis?
2. How much research has been done on DL-based OC data analysis from the perspective of each identified key feature?
3. How is AIA related to ML/DL-based cancer data analysis? What is the state of the existing DL-based OC data analyses from an AIA perspective?

The primary contributions of this survey are as follows:

- Identification of the key features of cancer data analysis and an overview of them, which are cancer-agnostic, can be used in any cancer-related ML/DL-based study;
- A comprehensive and systematic review of the existing DL-based analysis of OC data using the outlined features, including AIA and the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework-based systematic selection approach of existing studies;
- An overview of the open research challenges and future directions in DL-based OC data analysis.

The following sections of the paper are structured as follows. In Section 2, we provide an overview of a deep learning pipeline for data analysis and AIA, including AIA's six goals, and in Section 3, we present the procedures for investigating and selecting existing OC data analyses. We first identify the key features of cancer data analysis in Section 4, present an overview of each, and then present a summary of existing DL-based OC data analyses from the perspective of these characteristics and AIA. This section also provides an overview of AIA, including various aspects of it, and a mapping between the relevant key features of cancer data analysis and AIA. Next, we outline open research challenges and suggest future research directions in Section 5. Finally, Section 6 summarises the paper with our future work.

2. Background

2.1. DL pipeline for data analysis

A workflow pipeline, or simply a pipeline, refers to the sequence of steps and processes involved in developing and deploying a DL for a specific task or problem, such as cancer. Generally, it covers all stages, from data collection/gathering and pre-processing to model training, evaluation, and deployment (Echle et al., 2021; Zhang et al., 2019b; Hira et al., 2021). A well-structured pipeline helps streamline the development process, ensuring that the model performs effectively and efficiently. Fig. 1 presents a pipeline for developing DL-based data analysis. However, research studies generally do not incorporate the model deployment stage, and most studies discuss four steps or stages (e.g., data gathering, data preprocessing, model training, and validation). The following briefly presents the key steps of a DL-based data analysis.

1. **Use of Data Analysis:** Identifying the purpose or use of data analysis in any study is essential. Generally, DL-based data analysis is used for sample clustering, classification (e.g., malignant or benign), and predicting future values (e.g., cancer risk).
2. **Data Type and Modality Selection:** In this step, we need to identify the sources (e.g., for cancer, we can use data from a clinical or molecular source) of the data to be analysed and their modality (e.g., text, numeric, image).
3. **Data Gathering/Collection:** This step involves obtaining a dataset or datasets representative of the problem we want to solve. Data may come from a single source/database or multiple sources/multiple databases (e.g., cancer data may come from various clinics).
4. **Data Pre-processing:** Once the data are collected, it often requires pre-processing to make it suitable for training a DL algorithm. This may involve tasks such as data cleaning, normalisation, handling missing values, and feature engineering to extract meaningful information from raw data.

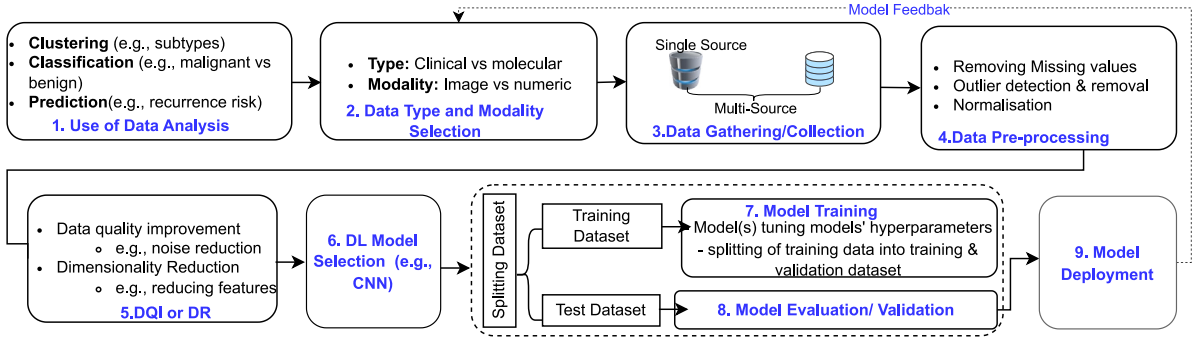

Fig. 1. DL pipeline for data analysis: key stages of DL-based data analysis.

5. **Data Quality Improvement (DQI) or Dimensionality Reduction (DR):** Improving training data quality or including additional information, especially quality or diversified images, can significantly improve cancer diagnostic performance (Wu et al., 2018; Zhang et al., 2019a; Meng et al., 2021). Also, we may need to reduce the dimensionality of datasets (Zhang et al., 2019b; Hira et al., 2021) to address dimensionality-related issues (e.g., the dimensionality curse).
6. **DL Model Selection:** This step involves choosing an appropriate DL architecture or algorithm for the task. Depending on the problem, we may choose from various architectures, such as CNNs for image tasks, recurrent neural networks (RNNs) for sequence data, or pre-trained models through transfer learning (an ML technique that allows the reuse of a pre-trained model on a new problem).
7. **Model Training:** First, we split the gathered dataset into training and test datasets before model training. After that, once a model or list of models is selected, we must build the models if they are not pre-trained, using the following 3 steps.

    (a) Model Building: In this step, we design and build the DL model(s) with the chosen architecture. The building process includes defining the model's architecture (e.g., layers, neurons, activation functions), specifying loss functions, and selecting optimisation algorithms (e.g., stochastic gradient descent).
    (b) Model Training: Training the DL model involves feeding it with the training data, iteratively updating the model's weights and biases to minimise the loss function through backpropagation and fine-tuning hyperparameters (e.g., learning rate, batch size). Training continues until the model converges or meets predefined criteria.
    (c) Hyperparameter Tuning: To optimise model performance, we use a validation/test dataset to perform hyperparameter tuning, including adjusting learning rates, dropout rates, and layer sizes to achieve the best results.

8. **Model Evaluation/Validation:** Once the model is trained, it must be evaluated/validated using the test dataset to assess its performance on unseen data. Common evaluation metrics include accuracy, precision, recall, F1 score, and mean squared error, depending on the type of problem.
9. **Model Deployment:** This is the final step of a DL pipeline where we deploy the evaluated/validated model in a real-life setting (e.g., use of a cancer detection model in a clinic). Deployment of the models also provides feedback to improve them.

A DL pipeline is an iterative process, and each step may need to be revisited and refined to improve model performance or adapt to changing requirements. Properly structuring and documenting the pipeline is crucial for creating robust and effective DL models.

2.2. AI assurance (AIA)

2.2.1. What is AIA and why do we need it?

AIA is a pivotal research field dedicated to safeguarding our society's fundamental pillars while developing and implementing advanced AI systems. AIA has recently gained renewed attention, and researchers, policymakers, and business leaders are using the term. However, despite its increasing usage, there is still no definitive agreement on its precise definition. According to Batarseh et al. (2021):

"A process that is applied at all stages of the AI engineering lifecycle, ensuring that any intelligent system is producing outcomes that are valid, verified, data-driven, trustworthy and explainable to a layman, ethical in the context of its deployment, unbiased in its learning, and fair to its users".

Although there is no globally accepted definition of AI assurance, the above definition is generic enough to capture most aspects of assurance. It is pertinent to all AI domains and subdomains. As nations are racing to develop AI-based solutions for almost every field, including medical and driverless cars, a race to progress in AI assurance is needed. Recently, the European Commission (EC) proposed rules and actions for excellence and trust for AI systems in the EU (EU, 2021), and the UK has established a roadmap for an effective AI assurance ecosystem (Centre for Data Ethics and Innovation, 2021). Also, very recently (BBC, 2021) OpenAI CEO called on the US Congress to regulate AI. Individual countries or continents are making some initiatives, but a global consensus is needed for adequate AI assurance.

Most existing AI systems have weaknesses in their ability to provide assurance, including the recently released Google Gemini AI tool (Kleinman, 2024). Therefore, unlike traditional software, assurance cannot be an afterthought in AI solutions. Instead, assurance should be by design and included in the overall learning process of any intelligent agent, algorithm, or environment (Freeman et al., 2022). In particular, all stakeholders (e.g., developers, users) (Centre for Data Ethics and Innovation, 2021) in an AI supply chain must play their role. Being AI developers/researchers, we can play an important role (as other stakeholders can contribute to AIA if there are trustworthy AI systems) in building an effective AI assurance ecosystem by embedding assurance in the design phase of the AI system.

AI assurance services will play a distinctive and vital role within AI governance (Centre for Data Ethics and Innovation, 2021). Setting standards and rules about how we expect AI systems to be used is not adequate. We must also have reliable information on whether they are following those rules. The following are a few reasons why we need AIA (Centre for Data Ethics and Innovation, 2021):

- Trust and Adoption: AIA builds trust. As we rely on safety certifications for cars or food, businesses and consumers need evidence that AI systems work effectively, safely, and ethically.
- Scientific Rigour: Assurance processes use reliable, standardised evidence to evaluate AI systems. Rigorous tests, performance assessments, and impact analyses provide scientific support for trustworthiness.

Table 1
Boolean search strings used for the journal databases.

Database	Boolean search strings
PubMed	(“Deep Learning”[MeSH Terms] OR “Deep Learning”[Title/Abstract] OR “Deep Neural Network”[Title/Abstract] OR “Convolutional Neural Network”[Title/Abstract] OR “CNN”[Title/Abstract] OR “Autoencoder”[Title/Abstract]) AND ((“ovarian neoplasms”[MeSH Terms] OR “ovarian cancer”[Title/Abstract] OR “epithelial ovarian cancer”[Title/Abstract] OR “serous ovarian cancer”[Title/Abstract] OR “high-grade serous carcinoma”[Title/Abstract] OR “low-grade serous carcinoma”[Title/Abstract] OR “endometrioid carcinoma”[Title/Abstract] OR “mucinous ovarian cancer”[Title/Abstract] OR “clear cell carcinoma”[Title/Abstract] OR “ovarian granulosa cell tumour”[Title/Abstract] OR “granulosa cell tumour of ovary”[Title/Abstract] OR “germ cell tumour”[Title/Abstract] OR (“teratoma”[MeSH Terms] OR “teratoma”[All Fields] OR “teratomas”[All Fields]) OR “embryonal carcinoma”[Title/Abstract] OR “choriocarcinoma”[Title/Abstract] OR “polyembryomas”[Title/Abstract] OR “gonadoblastoma”[Title/Abstract]))
Web of Science	“((TS=(ovarian cancer OR epithelial ovarian cancer OR serous ovarian cancer OR high-grade serous carcinoma OR low-grade serous carcinoma OR endometrioid carcinoma OR mucinous ovarian cancer OR ovarian granulosa cell tumour OR granulosa cell tumour of ovary OR ovarian theca cell tumour OR germ cell tumour OR teratoma OR embryonal carcinoma OR choriocarcinoma OR polyembryomas OR gonadoblastoma) AND TS = (Deep learning OR deep neural network OR Convolutional Neural Network OR CNN OR Autoencoder) NOT TS= (Comment OR editorial OR letter OR case reports)) AND PY=(2015–2023) and Meeting Abstract (Exclude – Document Types) and Editorial Material (Exclude – Document Types) and Proceeding Paper or Review Article (Exclude – Document Types)”
Scopus	(“Deep Learning” OR “Deep Neural Network” OR “Convolutional Neural Network” OR “CNN” OR “Autoencoder”) AND (“ovarian cancer” OR “epithelial ovarian cancer” OR “serous ovarian cancer” OR “high-grade serous carcinoma” OR “low-grade serous carcinoma” OR “mucinous ovarian cancer” OR “ovarian granulosa cell tumour” OR “granulosa cell tumour of ovary”) AND PUBYEAR > 2014 AND PUBYEAR < 2024 AND (LIMIT-TO (DOCTYPE, “ar”)) AND (LIMIT-TO (LANGUAGE, “English”))

- Economic Growth: A robust AIA ecosystem fosters innovation. By ensuring the reliability of AI, we unlock its full potential and create economic opportunities.

AIA that supports the governance of AI will maximise and reap the benefits of AI technologies while mitigating potential risks and harms (Department for Science, Innovation & Technology, 2024).

2.2.2. Main goals of AIA

Existing literature (Batarseh et al., 2021; Freeman et al., 2022) has identified six essential goals to achieve assurance in an AI system or solution:

1. **Ethical AI:** The respect of ethical principles throughout the development and deployment of an AI system.
2. **Fair AI:** Striving for fairness and equity, avoiding bias and discrimination in AI outcomes.
3. **Safe AI:** Safe AI refers to ensuring that an AI system operates reliably and without causing harm to humanity.
4. **Secure AI:** Addressing cybersecurity concerns related to an AI system, including data and models, safeguarding against attacks and vulnerabilities.
5. **Trustworthy AI:** Building confidence in AI systems by adhering to ethical standards, robustness, and reliability.
6. **XAI (Explainable AI)**: Explainable AI summarises the reasons for the model’s behaviour or produces insights about the causes of their decisions. On the contrary, interpretable AI refers to an AI system that describes the internals of a system in a way that is understandable to humans. In addition, interpretability and completeness are two potential ways to evaluate the explanations of an AI system (Gilpin et al., 2019).

Together, these goals can shape the path towards responsible and effective AI implementation. Multifaceted approaches, combining domain-specific and model-agnostic methods, are essential for achieving these goals, hence AIA.

3. Existing work selection strategies

We used the recent PRISMA guideline (Page et al., 2021) to systematically filter our search results. We identified 96 qualified scientific articles for the review study (Fig. 2). The selection started with 110 and 91 articles from the search results in the PubMed and Web of Science databases, respectively, using the Boolean search strings shown in Table 1. We also searched the Scopus database and found 2816 entries, but excluded them because random sampling showed that most were irrelevant.

Our study included all publications up to 20 May 2023, and 22 duplicate entries were removed from the two databases (Fig. 2). Subsequently, we screened the titles and abstracts of the publications, removing conference papers, editorials, perspectives, non-journal articles, other review and survey studies, and irrelevant studies that were not related to DL, OC, or humans. Subsequently, we identified 118 scientific studies to be evaluated for inclusion in this review study. Finally, after reviewing the list following the exclusion criteria, we found 96 journal articles to include in this study.

4. Result and discussion

Cancer is a very important and active domain (research and development-wise) of application of DL-based solutions. Many research works have been published in various subdomains (e.g. prediction, diagnosis, treatment) of individual cancers (e.g., ovarian cancer, lung cancer) and pancancer (Rajula et al., 2020; Zhang et al., 2019b). Existing ML/DL-based data analyses in cancer exhibit diversity in key features (e.g., analysis method, data type, ML/DL algorithms). Therefore, it is crucial to identify and review these key features to gain a comprehensive understanding of the field and contribute to future research, particularly from the perspective of individual cancers such as ovarian cancer. To make the features set generic (not specific to DL), we have identified and summarised them in Fig. 3 based on existing ML or DL-based data analyses (Cruz and Wishart, 2006; Kourou et al., 2015; Wong and Yip, 2018; Gulum et al., 2021). In the following subsections, we briefly discuss them individually with their status from existing DL-based ovarian cancer data analyses.

4.1. Subdomains of cancer and existing OC data analyses

Generally, any study based on ML/DL-based cancer data analysis can be categorised into one of the four subdomains: (i) prediction and prevention, (ii) detection and diagnosis, (iii) treatment and management, and (iv) prognosis. In the following, we briefly discuss them individually, including the cancer issues they address.

1. **Prediction and Prevention (PP)**: Prevention and early intervention are the most effective approaches to avoid psychological, physical, and economic suffering from cancer. However, such proactive intervention needs the ability to accurately anticipate an individual’s susceptibility or risk of cancer. ML/DL-based data analysis (Kim and Kim, 2018; Lu et al., 2020; Abdullah Alfayez et al., 2021) is useful for predicting the probability of developing cancer.

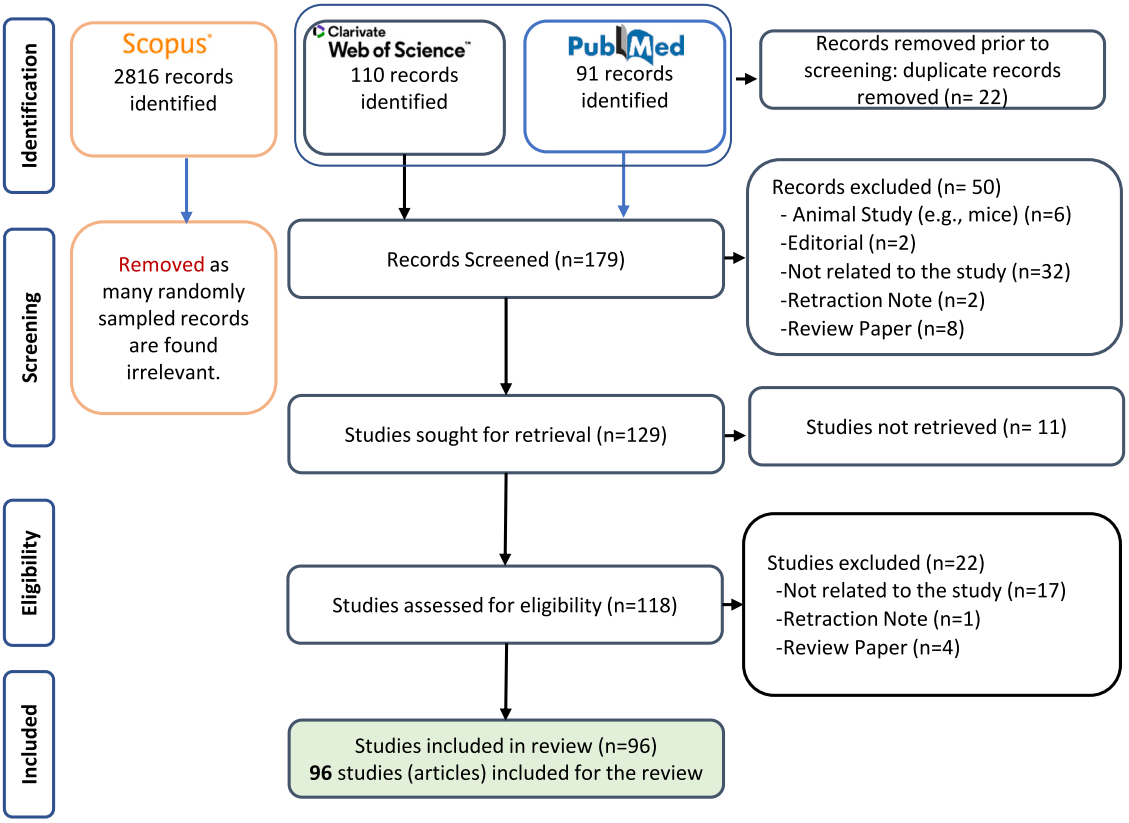

Fig. 2. PRISMA-based existing work selection strategies.

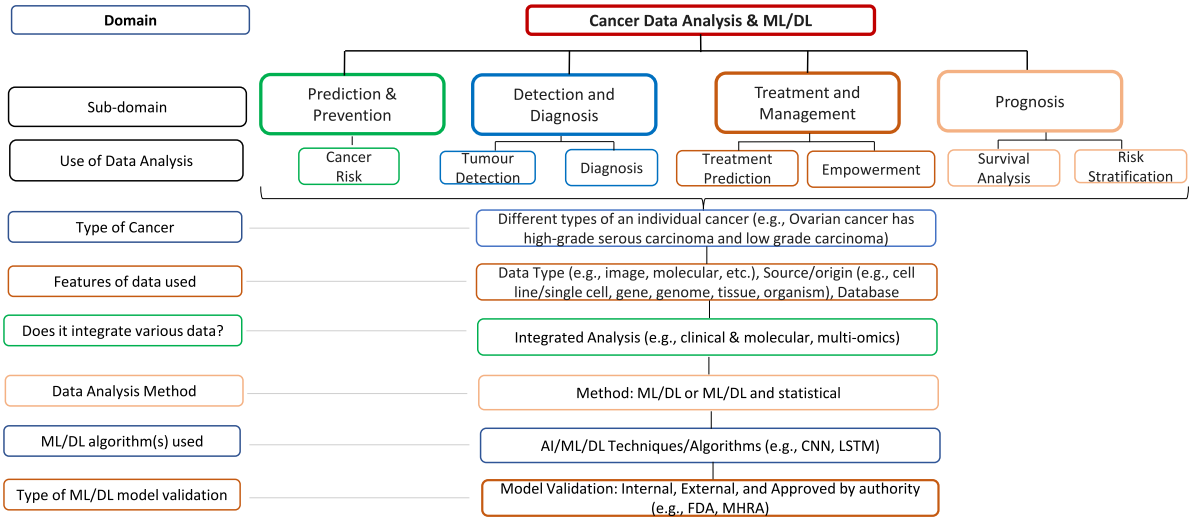

Fig. 3. Key features of existing ML/DL-based data analysis of cancer (**Acronyms:** CNN- Convolutional Neural Network, LSTM- Long Short Term Memory FDA- Food and Drug Administration, MHRA- Medicines and Healthcare products Regulatory Agency).

2. **Detection and Diagnosis (DD)**: This is the most active sub-domain of cancer (Cruz and Wishart, 2006; Kourou et al., 2015; Patel et al., 2020; Gulum et al., 2021) where ML or DL are used to screen, detect and diagnose the disease. Work in this sub-domain mainly uses ML/DL to analyse data from one of the three stages or types of diagnosis: (i) lab-test based (Islam et al., 2021), (ii) imaging-test based (e.g., radiomics-driven diagnosis) (Giger, 2018; Akazawa and Hashimoto, 2020), and (iii) biopsy-based (e.g., histopathological image analysis-based diagnosis) (Komura and Ishikawa, 2018; Echle et al., 2021), with an aim to assist clinicians in informed-decision making.
3. **Treatment and Management (TM)**: Resistance to therapy is a leading cause of cancer treatment failure, resulting in many cancer-related deaths. The existing treatment procedure is based primarily on cancer subtypes and genetic modifications. However, the existence of a genetic modification does not necessarily indicate the therapeutic response. Also, the response may differ depending on the cancer subtype. As a result, an integrated study is needed to identify optimal treatment plans or therapies for a patient. ML/DL-based predictive models can use integrated data to predict treatment response (e.g., Hwangbo et al., 2021; Wang et al., 2022b) for individuals or groups and identify a

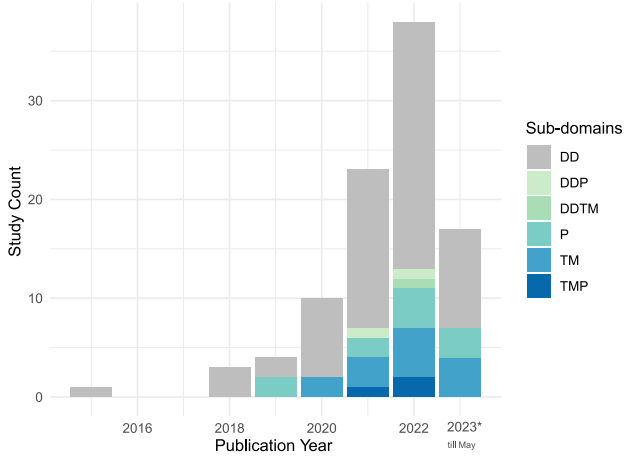

Fig. 4. Yearly published studies (**Acronyms:** DD-Detection and Diagnosis, TM- Treatment and Management, P-Prognosis, DDP-DD and P, DDTM- DD and TM, TMP- TM and P).

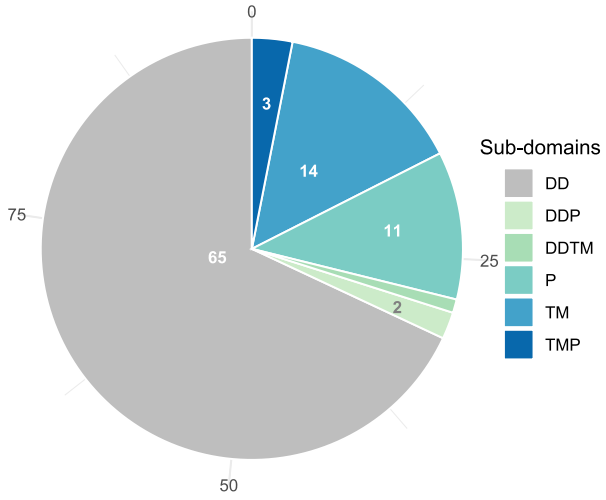

Fig. 5. Sub-domain wise distribution of existing studies (see Fig. 4 for the acronyms).

personalised and effective treatment. Importantly, these models (Sun et al., 2020; Boniolo et al., 2021) aid researchers and the industry in developing and designing cancer drugs to promote precision oncology (PO). Additionally, utilising PO in conjunction with ML/DL-based stratification (Patel et al., 2020) will empower oncologists and ML/DL-based data analysis (e.g., behaviour, lifestyle, social media data De Silva et al., 2018b) can aid patients in managing their cancer.

4. **Prognosis (P)**: Prognosis in cancer is another active sub-domain of ML and DL (Cruz and Wishart, 2006; Kourou et al., 2015; Gulum et al., 2021). In this sub-domain, ML or DL are used for (i) survival analysis (e.g., Avesani et al., 2022; Hira et al., 2021), (ii) cancer recurrence prediction (e.g., Xu et al., 2020), and (iii) residual disease prediction (e.g., Meti et al., 2021). Survival analysis (SA) includes survival risk stratification (Tseng et al., 2020) and the prognosis, such as disease-specific or overall survival (OS) after a diagnosis or therapy. On the other hand, cancer recurrence prediction estimates the likelihood of redeveloping, and residual disease prediction estimates cancer cells that remain after surgery.

Subdomains of Existing OC Data Analyses: Figs. 4 and 5 summarise subdomains of the existing OC data analyses and yearly published studies in each domain. Also, Tables 2, 3, and 4 respectively summarise the existing studies on DD, TM and P in terms of the identified key features[2] of cancer data analysis and AIA. Fig. 4 illustrates that most studies (95 out of 96) were published between 2018 and 2023, with a gradual increase in the published studies in the respective subdomains, and this could be due to the recent advancement in DL technologies. In Fig. 5, analysis distribution shows that 67.7% (65 out of 96) focused on DD (e.g., Chen et al., 2022; Saida et al., 2022), 11.45% (11 out of 96) on P (e.g., Kim et al., 2021; Zhu et al., 2021; Wang et al., 2023a), 14.6% (14 out of 96) on TM (e.g., Wang et al., 2022b; Han et al., 2022), while the remaining 6 out of 96 covered mixed subdomains (e.g., DDP-DD and P, DDTM- DD and TM). In particular, the PP subdomain lacked work based on DL, except for a few studies based on ML (Kim and Kim, 2018, 2014). The scarcity of publications in this subdomain and the lower number of studies in the P and TM subdomains, in contrast to DD, can be attributed to the inaccessibility of relevant datasets.

4.2. Use of data analysis and existing OC data analyses

The Use of Data Analysis (UDA) in cancer can be grouped into one or a combination of the four capabilities: prediction (e.g., risk prediction, survival prediction), classification (e.g., subtypes, therapy stratification), association/clustering (e.g., subtypes clustering, dimensionality reduction), and optimisation. However, existing cancer studies generally analyse data to do the first three.

USA of Existing OC Data Analyses: As the distribution reveals in Fig. 6, 45.83% (44/96) studies used data analysis to classify (C) cancer-related activities (e.g., subtype classifications Hira et al., 2021, treatment stratification Guo et al., 2020) and 34.4% (33 out of 96) to improve data quality and classify (DQIC) (e.g., dimensionality reduction Hira et al., 2021, data compression AlShibli and Mathkour, 2019, style change Shin et al., 2021). Furthermore, 10.4% (10/96) studies used data analysis to predict or perform survival analysis (Hao et al., 2019). The remaining 9 out of 96 studies were mainly used for data quality improvement, including one for cancer data generation (CDG Levine et al., 2020).

4.3. Cancer types and existing OC data analyses

Generally, cancer experiences intertumour and intratumour heterogeneity (Marusyk and Polyak, 2010; Marusyk et al., 2012; Bedard et al., 2013; Dagogo-Jack and Shaw, 2018). Due to this heterogeneity, for any cancer (e.g., ovarian cancer), different tumour cells could exhibit different morphological and phenotypic characteristics, including cellular morphology, gene expression, proliferation, and metastatic possibility (Marusyk and Polyak, 2010). For example, ovarian carcinomas show various neoplasms with different risk factors, precursor lesions, aetiology, spread patterns, molecular profiles, clinical procedure, response to treatment, and prognosis (De Leo et al., 2021). Therefore, cancer typing or subtyping using cancer's pathological and molecular characteristics is essential for individualised clinical decision-making (Rafique et al., 2021). Based on histopathology, immunoprofile, and molecular analysis, the WHO (World Health Organisation) identified at least five major types of ovarian carcinoma: high-grade serous carcinoma (HGSC or HGSOC), endometrioid carcinoma (EC), clear cell carcinoma (CCC), low-grade serous carcinoma (LGSC or LGSOC) and mucinous carcinoma (MC) (De Leo et al., 2021). Existing ML/DL-based OC data analysis addresses one or more of these five types.

Cancer Types of Existing OC Data Analyses: As observed in Fig. 7, the majority of existing data analyses related to ovarian cancer only focus on ovarian cancer or ovarian cancer in combination with one or more other cancers (OCO). Out of 96 studies, 80.2% (77/96) studies

[2] Please see the respective section for the definition or a brief description of the acronyms or their elaborated terms.

Table 2
DL-based data analysis for ovarian cancer detection and diagnosis.

Analysis	CST	Use-of-DA	Data features			Integrated analysis			Analysis Methods & DL details			VM	AIA
			Source	Format	Repository	Data	Level	Method	AM	LT	Algorithms		
Chen et al. (2022)	OC	C	C	IM1	SCD	CDI	FDeLI	NF-NBY1	DL	SL	CNN	IV	
Saida et al. (2022)	EOC	C	C	IM1	SCD				DL	SL	CNN	IV	
Hira et al. (2021)	HGSOC	DQICCl	CO	TN	MCD1	CODI	FLI	NF-NBY2	Hybrid2	UL&SL	VAE&DNN	IV	
Avesani et al. (2022)	HGSOC	SA	C	IM1	MCD1	CDI	FLI	NF-NBY1	Hybrid2	SL	CNN	EV1	
Hu et al. (2023)	EOC	DQI	C	IM1	MCD1				DL	SL	CNN	IV	
Wang et al. (2023d)	EOC	DQIC	C	IM1	SCD				Hybrid2	SL	CNN	IV	
Gangadhar et al. (2023)	OC	C	C	IM3	SCD				DL	SL	CNN	IV	
Wang et al. (2023c)	OC	C	C	IM1	MCD1				DL	SL	CNN	IV	
Gajjela et al. (2023)	OC	C	C	IM3	SCD				Hybrid1	SL	CNN	IV	
Wei et al. (2023)	EOC	C	C	MM	MCD2	CDI	DeLI	NF-NBY3	Hybrid2	SL	CNN	EV2	
Boyanapalli and Shanthini (2023)	OC	C	C	IM1	MCD1				Hybrid2	SL	CNN	IV	
Wang et al. (2022d)	OC	C	C	IM2	SCD				DL	SL	CNN	IV	
Kodipalli et al. (2023)	OC	C	C	IM1	SCD				Hybrid1	UL&SL	CNN	IV	
Wang et al. (2023e)	OC	DQIC	C	IM1	SCD				DL	SL	CNN	IV	
Ho et al. (2023)	HGSOC	DQIC	C	IM2	SCD				DL	SL	DNN	IV	
Hema et al. (2022)	OC	DQIC	C	IM3	MCD1				DL	SL	CNN	IV	
Hsu et al. (2022)	OC	DQIC	C	IM1	SCD				Hybrid2	SL&TL	CNN	IV	
Bahado-Singh et al. (2022)	OC	C	O	TN	SCD				Hybrid1	SL	DNN	IV	
Wang et al. (2022c)	OC	C	C	IM1	SCD				DL	SL	CNN	IV	
Nero et al. (2022)	EOC	DQIC	C	IM2	SCD				DL	SL	CNN&Tr	IV	
Jung et al. (2022)	OC	C	C	IM1	SCD				DL	UL&SL	AE&CNN	IV	
Mayer et al. (2022)	HGSOC	C	C	IM2	MCD2				Hybrid2	SL	CNN	EV2	
Farahani et al. (2022)	OC	DQIC	C	IM2	MCD2				DL	SL&TL	CNN	EV2	
Wu et al. (2022)	OC	C	O	MM	MCD1				DL	SL	CNN	IV	
White et al. (2022)	OCO	DQIC	C	MM	MCD2				DL	UL&SL	AE&CNN	EV2	XAI
Reilly et al. (2022)	OC	C	C	TN	SCD	CDI	FLI	NF-NBY1	DL	SL	MIA3G	IV	
Sun et al. (2022)	OC	DQIC	O	TN	MCD2	ODI	FLI	NB-NBY	DL	SL	GCN	IV	
Gao et al. (2022)	OC	C	C	IM1	MCD1				DL	SL	CNN	EV1	
Sengupta et al. (2022)	OC	C	C	MM	SCD	CDI	DeLI	NF-BY	DL	SL	CNN	IV	
Jian et al. (2022)	EOC	C	C	IM1	MCD1				Hybrid2	SL	CNN	IV	
Jeong et al. (2022)	OCO	DQI	O	TN	MCD1				DL	SL	CNN	IV	
Jeya Sundari and Brintha (2023)	OC	DQIC	C	IM2	MCD2				DL	SL	CNN&MBiLSTM	IV	
Ramasamy and Kaliyaperumal (2023)	OC	DQIC	C	IM2	MCD1				DL	SL	CNN	IV	
Kodipalli et al. (2022)	OC	C	C	IM1	MCD1				DL	SL	CNN	IV	
Jiang et al. (2022)	HGSOC	DQIC	C	IM2	SCD				Hybrid2	SL	CNN	IV	
Ahn et al. (2022)	OCO	CCl	O	TN	MCD1				DL	SL	DNN	IV	
Petrovsky et al. (2021)	OCO	C	O	MM	SCD	ODI	FLI	NF-NBY1	DL	SL	CNN	IV	
Qazi and Raza (2021)	OC		O	TN	MCD2				DL	SL	DNN	IV	
Jian et al. (2021)	EOC	C	C	IM1	SCD				DL	SL	CNN	IV	
Ye et al. (2021)	OC	C	O	TN	MCD2	ODI	FLI	NB-BY	DL	UL&SL	GAT&DNN	IV	
Meng et al. (2021)	OC	DQIC	C	IM2	MCD1				DL	SSL&SL	GAN&CNN	IV	
Pastuszak et al. (2021)	OC	C	CO	IM3	MCD2				DL	SL	DNN	IV	
Xie et al. (2021)	OCO	C	C	IM1	SCD	CDI	FLI	NF-NBY1	DL	SL	CNN	IV	
González et al. (2021)	OC	DQIC	O	MM	MCD1				DL	SL	CNN	IV	
Shin et al. (2021)	OC	DQIC	C	IM2	MCD2				DL	UL&SL	GAN&CNN	EV2	
Christiansen et al. (2021)	OC	C	C	IM1	MCD1				DL	SL&TL	CNN	IV	
Wang et al. (2021)	OC	C	C	MM	SCD	CDI	DeLI	NF-NBY2	DL	SL	DNN	IV	
Ghoniem et al. (2021)	OC	C	CO	MM	MCD1	CODI	DeLI	NF-NBY1	DL	SL	CNN&LSTM	IV	
Gupta et al. (2021)	OCO	C	CO	TN	MCD2				Hybrid1	SL	DNN	IV	
Kopylov et al. (2021)	OCO	DQIC	O	TN	SCD				DL	UL&SL	CNN	IV	
Chen et al. (2021)	OC	DQIC	CO	TN	SCD	CODI	FLI	NF-NBY1	Hybrid1	UL&SL	GCN	IV	
Mohammed et al. (2021)	OCO	DQIC	O	TN	MCD1				Hybrid2	UL&SL	CNN	IV	
Guo et al. (2020)	OC	CCl	O	TN	MCD2	ODI	FLI	NF-NBY1	Hybrid2	UL&SL	AE	EV2	
Tanabe et al. (2020)	EOC	DQIC	C	TN	SCD	CDI	FLI	NF-NBY1	DL	SL	CNN	IV	
Basharat et al. (2020)	OC	DQIC	O	IM3	MCD2				DL	SL	CNN	IV	
Urase et al. (2020)	OC	DQIC	C	IM2	MCD1				Hybrid2	SL	CNN	IV	
Kilicarslan et al. (2020)	OCO	DQIC	O	TN	MCD1				Hybrid1	UL&SL	AE& CNN	IV	
Zhao et al. (2020)	OCO	DQIC	O	TN	MCD2				DL	SL	CNN	EV2	
Mallavarapu et al. (2020)	OCO	Cl	O	TN	MCD1	ODI	FLI	NB-NBY	Hybrid1	UL& SL	RBM& DBN	IV	
Levine et al. (2020)	OCO	CDG	C	IM2	MCD2				DL	UL&SL	GAN&CNN	IV	
Klein et al. (2019)	EOC	C	C	IM3	SCD				Hybrid1	SL	CNN	IV	
AlShibli and Mathkour (2019)	OCO	C	O	TN	MCD2				DL	SL	CNN	IV	
Vázquez et al. (2018)	OC	C	C	TN	MCD1	CDI	FLI	NF-NBY2	Hybrid2	SL	RNN	IV	
Du et al. (2018)	OCO	DQIC	C	IM2	MCD1				DL	SL&TL	CNN	IV	
Wu et al. (2018)	OC	DQIC	C	IM2	SCD				DL	SL	CNN	IV	

(*continued on next page*)

Table 2 (*continued*).

Liang et al. (2015)	OCO	SA	CO	TN	MCD2	CDI	FLI	NF-NBY2	DL	UL&SL	DBN	IV
Irajizad et al. (2022)	OC	C	O	TN	MCD1				Hybrid2	SL	DNN	EV1
Li et al. (2022)	OC	DQIC	C	IM2	SCD				DL	SL	CNN	IV

Acronyms: CST- Cancer Subtype, DA- Data Analysis, AM- Analysis Method, LT- Learning Technique, VM- Validation Method, AIA- AI Assurance, OC- Ovarian Cancer, EOC- Epithelial Ovarian Cancer, HGSOC- High-grade Serous Carcinoma, OCO- OC and others, C- Classification/Clinical, Cl- Clustering, DQI-Data Quality Improvement, DQIC- DQI and Classification, DQICCl-DQIC and Clustering, SA- Survival Analysis, O- Omics, CO- Clinical and Omics, IM- Image (1- Radiological, 2- Histopathological, 3- Others), TN- Text or Numeric, SCD - Single-centred Dataset, MCD-Multi-centred Dataset (1- same country, 2- different countries), CDI- Clinical Data Integration, ODI- Omics Data Integration, CODI- Clinical and ODI, DeLI- Decision Level Integration, FDI- Feature Level Integration, FDeLI- Feature and DeLI, NB-NBY- Network-based non-Bayesian, NF-NBY-Network Free Non Bayesian (1- concatenation, 2- correlation, 3- ensemble), NB-BY- Network-based Bayesian, NF-NB- Network-free Bayesian, Hybrid1- ML and DL, Hybrid2- DL and Statistical, SL- Supervised Learning, UL- Unsupervised Learning, SSL- Semi-Supervised Learning, TL- Transfer Learning, CNN- Convolutional Neural Network, DNN- Deep Neural Network, AE- Autoencoder, VAE- Variational AE, MIA3G- Multivariate Index Assay 3G, RBM- Restricted Boltzmann Machine, LSTM- Long Short-Term Memory, MBiLSTM- Multi-Branch Bidirectional LSTM, GAN- Generative Adversarial Network, GAT- Graph Attention Network, RNN- Recurrent Neural Network, GCN- Graph Convolutional Network, DBN- Deep Belief Network, IV- Internal Validation, EV- External Validation (1- different source but same country, 2- different source and countries), XAI- Explainable AI.

Table 3
DL-based data analysis for ovarian cancer TM.

Analysis	CST	Use-of-DA	Data features			Integrated analysis			Analysis Methods & DL details			VM	AIA
			Source	Format	Repository	Data	Level	Method	AM	LT	Algorithms		
Wang et al. (2022b)	EOC	C	C	MM	MCD1				DL	SSL&SL	CNN	IV	
Han et al. (2022)	OC	DQIC	C	IM2	MCD2	CDI	FLI	NF-NBY2	DL	SSL&SL	CNN	IV	
Hwangbo et al. (2021)	HGSOC	C	C	TN	MCD1	CDI	FLI	NF-NBY1	Hybrid2	SL	DNN&O	IV	
Sun et al. (2020)	OCO	C	C	TN	MCD2				DL	SL	DNN	IV	
Reilly et al. (2023)	OC	C	C	IM3	MCD1				DL	SL	MIA3G	IV	
Wang et al. (2023a)	EOC	DQIC	C	MM	MCD1				Hybrid2	SL	CNN	IV	
Wang et al. (2023b)	EOC	DQIC	C	IM2	MCD1				Hybrid2	SSL&SL	FCN&CNN	IV	XAI
Nasimian et al. (2023)	OC	DQIC	O	TN	MCD2				Hybrid1	SL	TabNet	IV	XAI
Laios et al. (2022a)	HGSOC	C	C	MM	SCD	CDI	FLI	NF-NBY2	Hybrid1	SL	DNN	IV	
Laios et al. (2022b)	EOC	C	C	TN	SCD	CDI	FLI	NF-NBY1	Hybrid1	SL	DNN&O	IV	XAI
Wang et al. (2022a)	HGSOC	C	C	IM2	MCD1				DL	SSL&SL	FCN	EV1	
Laury et al. (2021)	HGSOC	C	C	IM1	SCD				DL	SL	DNN	IV	
Liu and Xie (2021)	OCO	C	CO	TN	MCD2	CODI	FLI	NF-NBY1	DL	UL&SL	CNN	IV	XAI
Yu et al. (2020)	OC	C	CO	MM	MCD1	CODI	FLI	NF-NBY2	DL	SL	CNN	IV	
Lei et al. (2022)	EOC	DQIC	C	MM	SCD	CDI	FLI	NF-NBY2	Hybrid1	UL&SL	CNN	IV	
Bote-Curiel et al. (2022)	OC	DQIC	CO	TN	MCD1	CODI	FLI	NF-NBY1	DL	UL	AE	IV	XAI

Acronyms: CST- Cancer Subtype, DA- Data Analysis, AM- Analysis Method, LT- Learning Technique, VM- Validation Method, AIA- AI Assurance, OC- Ovarian Cancer, EOC- Epithelial Ovarian Cancer, HGSOC- High-grade Serous Carcinoma, OCO- OC and others, C- Classification/Clinical, Cl- Clustering, DQI-Data Quality Improvement, DQIC- DQI and Classification, DQICCl-DQIC and Clustering, SA- Survival Analysis, O- Omics, CO- Clinical and Omics, IM- Image (1- Radiological, 2- Histopathological, 3-Others), TN- Text or Numeric, SCD - Single-centred Dataset, MCD-Multi-centred Dataset (1- same country, 2- different countries), CDI- Clinical Data Integration, ODI- Omics Data Integration, CODI- Clinical and ODI, FLI- Feature Level Integration, NB-NBY- Network-based non-Bayesian, NF-NBY-Network Free Non Bayesian (1- concatenation, 2- correlation, 3- ensemble), NB-BY- Network-based Bayesian, NF-NB- Network-free Bayesian, Hybrid1- ML and DL, Hybrid2- DL and Statistical, SL- Supervised Learning, UL- Unsupervised Learning, SSL- Semi-Supervised Learning, TL- Transfer Learning, CNN- Convolutional Neural Network, DNN- Deep Neural Network, O- others, AE- Autoencoder, MIA3G- Multivariate Index Assay 3G, TabNet- Attentive Interpretable Tabular Learning, RNN- Recurrent Neural Network, FCN- Fully Connected Network, DCAS- DeepConvAttentionSurv, DeepCox- Deep Learning and Cox regression, IV- Internal Validation, EV- External Validation (1- different source but same country, 2- different source and countries), XAI- Explainable AI.

Table 4
DL-based data analysis for OC prognosis (P).

Analysis	CST	Use-of-DA	Data features			Integrated analysis			Analysis methods & DL details			VM	AIA
			Source	Format	Repository	Data	Level	Method	AM	LT	Algorithms		
Kim et al. (2021)	EOC	SA	C	TN	SCD	CDI	FLI	NF-NBY1	DL	SL	DNN	IV	
Zhu et al. (2021)	HGSOC	DQISA	CO	MM	MCD2	CODI	FLI	NF-NBY1	DL	UL&SL	CNN	IV	
Wang et al. (2023a)	OC	SA	C	IM2	MCD1				DL	SSL	CNN	IV	
Liu et al. (2023)	HGSOC	DQISA	C	IM1	SCD	CDI	FLI	NF-NBY2	Hybrid2	SL	CNN	IV	
Zhang et al. (2023)	HGSOC	SA	CO	TN	MCD2				Hybrid1	UL&SL	DNN&O	EV2	
Zheng et al. (2022)	HGSOC	SA	C	MM	SCD	CDI	FLI	NF-NBY1	Hybrid2	SL	RNN	IV	
EOCSA (2022)	EOC	C	C	IM2	MCD1				Hybrid2	SL	DCAS	IV	
Liu et al. (2022a)	OC	SA	O	TN	MCD1				Hybrid2	SL	DeepCox	IV	
Yokomizo et al. (2022)	OC	DQIC	C	IM2	SCD				DL	SL	CNN	IV	
Tong et al. (2021)	OCO	SA	CO	TN	MCD1	ODI	FLI	NF-NBY1	Hybrid2	UL&SL	AE	IV	
Hao et al. (2019)	OCO	SA	CO	TN	MCD2	CODI	FLI	NB-NBY	Hybrid2	SL	DNN	IV	
Wang et al. (2019)	HGSOC	SA	C	MM	MCD1	CDI	FLI	NF-NBY1	Hybrid2	SL	DNN	EV1	

See the acronyms in the notes of Table 3

(e.g., Hira et al., 2021; Wang et al., 2019 focused on ovarian cancer, while the remaining 19.8% (19/96) studies (e.g., Zhang et al., 2019b; Hao et al., 2019) are focused on OCO. However, we found that most studies (47/77) on ovarian cancer (e.g., Wang et al. (2023a) and Liu et al. (2022a)) did not explicitly mention the type of ovarian carcinoma being studied, such as HGSOC or EOC (Epithelial Ovarian Cancer). In contrast, only 16.67% (16/96) of studies mentioned EOC as their type, and 14.6% (14/96) of studies (e.g., Hira et al. (2021)) mentioned HGSOC, considered the most dangerous subtype of ovarian carcinoma.

4.4. Data features and existing OC data analyses

Data are at the heart of any data analysis. The results of a data analysis depend on the used dataset's features and quality (Kim et al., 2016). The key features of the data used in the analysis of cancer data based on ML/DL can be discussed from three perspectives (presented in Fig. 8) (i) data types (based on sources), (ii) data types (based on data formats), and (iii) data repositories. In addition to these key characteristics, the data could be structured (e.g. laboratory tests, mRNA expression) and unstructured (e.g. clinical notes, reports) (Zhang et al.,

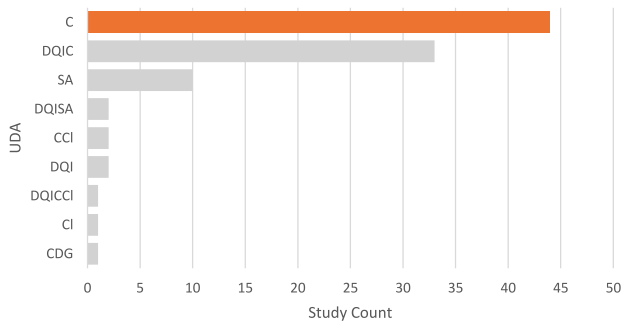

Fig. 6. Use of Data Analysis (UDA) in existing OC data analyses (**Acronyms**: C- Classification, Cl- Clustering, DQI-Data Quality Improvement, DQIC- DQI and Classification, DQICCl- DQIC and Clustering, SA- Survival Analysis).

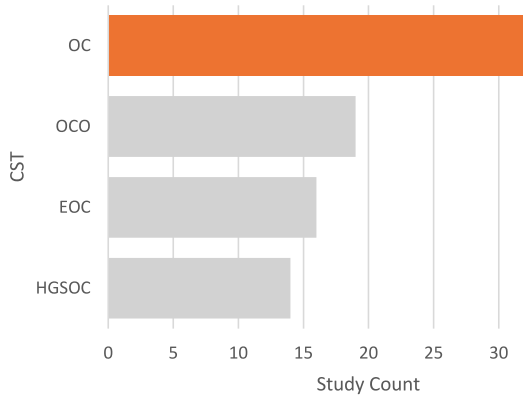

Fig. 7. Ovarian cancer subtype of existing studies (**Acronyms**: OC- Ovarian Cancer (no specific sub-type mentioned), OCO- OC and Other cancer (e.g., Breast), EOC- Epithelial Ovarian Cancer, HGSOC- High-grade Serous Carcinoma).

2020). Generally, data preparation techniques take care of unstructured data and convert them into analysable or structured forms.

As shown in Fig. 8, source-based data can be (i) environmental and lifestyle data (Kim and Kim, 2018; Abdullah Alfayez et al., 2021), (ii) clinical data (Islam et al., 2021; Vázquez et al., 2018; Echle et al., 2021), and (iii) biological, especially omics data (Hira et al., 2021; Zhang et al., 2019b). Similarly, cancer-related data can be in one of three formats: (i) text or numeric (Islam et al., 2021; Hira et al., 2021; National Cancer Institute, 2019), (ii) image (Gao et al., 2022; Echle et al., 2021) and (iii) multimodal or hybrid (Komura and Ishikawa, 2018; Echle et al., 2021). In cancer data analysis, most of the existing work relies on secondary data from repositories since primary data collection for ML/DL models is time-consuming and sometimes complex due to ethical clearance. Using data from well-maintained and trusted repositories is recommended, as there are many repositories. Fig. 8 provides a few examples of widely used repositories and examples for each data type (both source- and format-based).

Data Features of Existing OC Data Analyses: Data features of existing studies are analysed from the data types, data formats, and repositories and summarised as below:

1. **Data Types:** Fig. 9 summarises the existing studies' data types (source) and their corresponding data formats. As depicted in the diagram, most studies (65.6% (63 of 96)) used clinical data (C) for their investigations. The omics data (O) was used in 20.8% (20/96) of the studies, while a smaller portion, 13.5% (13/96) of the studies, used data from clinical and omics (CO) sources in their analyses. The availability of relevant and accessible datasets is a predominant factor contributing to the prevalence of clinical data-driven studies, accounting for 79% (76/96) of the studies.
2. **Data Formats**: Fig. 9 illustrates that the predominant data format used in existing studies is images, accounting for 50% or 48 out of 96 studies. In particular, 96% (46 out of 48) of these images originate from clinical sources such as Radiological/IM1 (Hu et al., 2023; Laury et al., 2021; Liu et al., 2023), pathomics or histopathological images/IM2 (Wang et al., 2022d, 2023b,a), and other types such as mass spectrometry (Reilly et al., 2023; Pastuszak et al., 2021)). Of the remaining 50% (48/96) of studies, 64% (32/50) use text or numeric (TN) data, which are drawn from all three sources but are predominantly from omics. Among these, the rest, 16.67% (16/96), integrate multimodal (MM) data, combining elements like images and text in their analyses. The prevalence of image data is primarily due to the availability of clinical imaging equipment and the advancement of DL-based image processing.
3. **Repository/Databases of Existing Studies**: Generally, repositories/databases used in cancer studies can be single-centred (SCD) (e.g., one clinic or hospital) or multi-centred (MCD), with data coming from multiple clinics or hospitals. In this study, we have further divided MCD into MCD1 and MCD2 to visualise the heterogeneity of the data sources or databases used. MCD1 means the data come from multiple centres or clinics and the same country or demography. In the case of MCD2, the data come from different clinics/centres and multiple countries or demography.
   Figs. 10 and 11 visually show the distribution of the studies in terms of these three types of databases (SCD, MCD1 and MCD2) for the data sources and formats. As seen in Figs. 10 and 11, most of the studies (63. 5% or 61/96) used MCD (e.g., Tong et al., 2021; Hao et al., 2019), and the remaining 36.5% (35/96) studies used SCD. However, most multi-centred studies (60.65% or 37/61) rely on data from two or more centres but are limited to a country or population, which could make the DL models or solution biased to that population, limiting the clinical deployment of the solution. In the case of clinical data (C), the distribution of the SCD and MCD study is well balanced (31 vs 32 or 49.2% vs 50.8%), while most (88% or 29/33) of the omics and CO (clinical and omics) data-based analyses used MCD. However, in Fig. 11, it is evident that the distribution of existing studies in terms of data formats and their associated databases or repositories exhibits heterogeneity. For example, among image-based studies, SCD was used by 45. 8% (22/48), MCD1 (e.g., Tong et al. (2021)) by 37.8% (18/48), and the remaining 16. 67% (8/48) used MCD2 (e.g., Hao et al. (2019)). In contrast, in the case of studies that rely on TN and MM data, the majority, with 73% (35/48), used MCD, while the remaining 13 studies used SCD. Most of these data repositories (Fig. 8) are publicly accessible (CDC, 2021; NIH, 2023; TCIA, 2024; UCSC, 2020; ICGC, 2019; CCLE, 2020).

4.5. Integrated analysis and existing OC data analyses

Cancer is characterised by inter-tumour and intra-tumour heterogeneity (Dagogo-Jack and Shaw, 2018), which disrupts cellular processes at various molecular levels, such as DNA, RNA, proteins, and metabolites (Hu et al., 2013). As a result of its heterogeneity, different cancerous tumour cells can display various morphological and phenotypic characteristics (Marusyk and Polyak, 2010). Hence, analysis using one type of clinical data (e.g., image or blood test results) may not accurately diagnose the disease. Also, molecules at various levels are interconnected in modifying cellular functions (Hu et al., 2013; Cheng and Zhan, 2017). Therefore, an analysis that only focuses on one level is not enough to fully comprehend the complex nature of cancer. To diagnose and fully understand the cellular defects that cause and contribute to cancer, an integrated analysis of data from various clinical

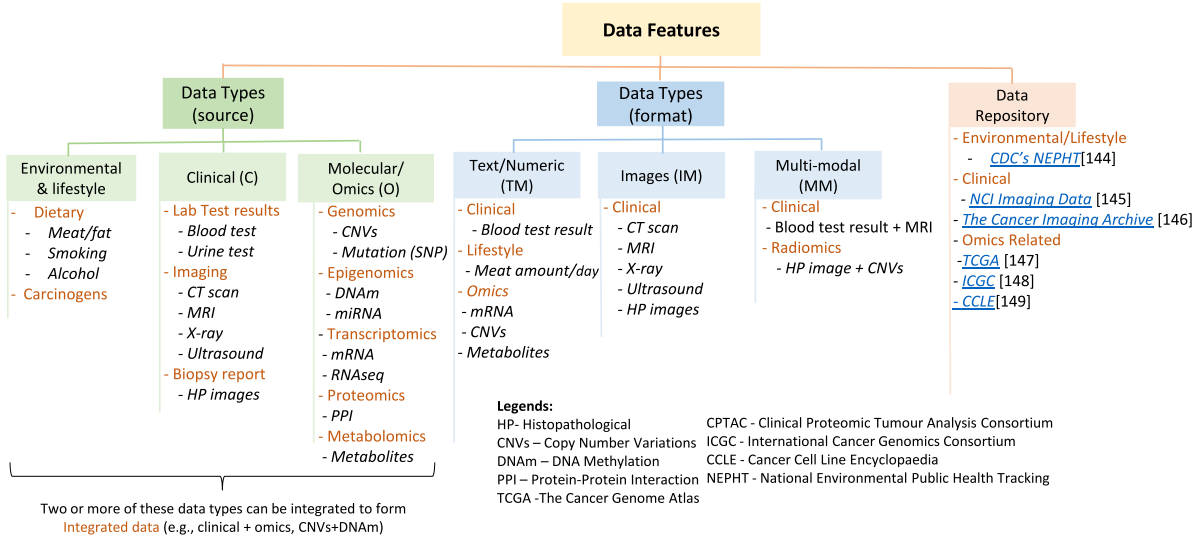

Fig. 8. Key features of data used in existing data analysis of cancer.

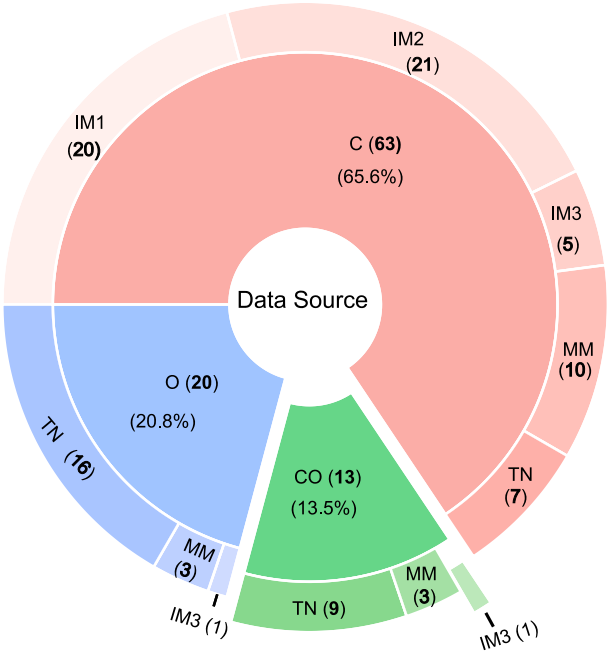

Fig. 9. Data-type (source) and Data-type (format) of Existing Studies (**Acronyms**: O- Omics, C- Clinical, and CO- Clinical and Omics, IM- Image (1-Radiological, 2-Histopathological, 3-Others), TN- Text or Numeric, MM- multimodal (e.g., image and text)).

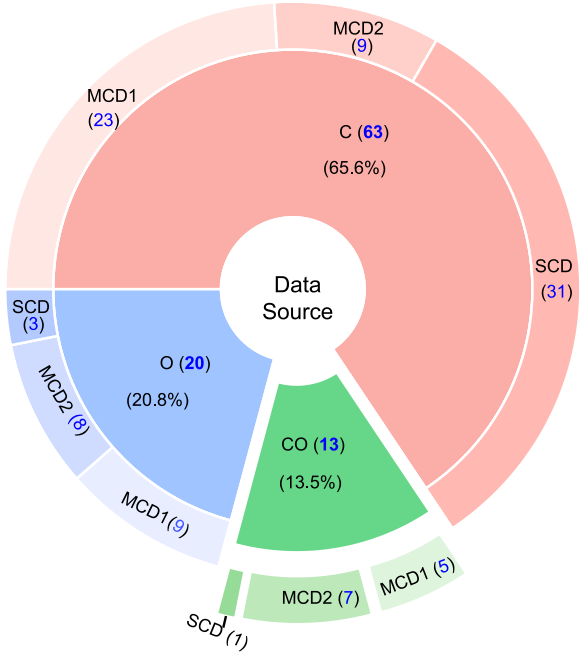

Fig. 10. Data-type (source) and Repository of existing studies (**Acronyms**: O- Omics, C-Clinical, and CO- Clinical and Omics, SCD - Single-centred Dataset, MCD- Multi-centred Dataset (1-same country, 2-different countries)).

and "omics" levels is necessary. Data integration for cancer analysis, especially the integration of omics data and the corresponding analysis, is a very active research area (Huang et al., 2017; Zhu et al., 2017; Chakraborty et al., 2018; Wu et al., 2019; Subramanian et al., 2020; Zanfardino et al., 2021; Jendoubi, 2021). Many research papers have been published in this area.

Currently, integrated studies typically combine data from multiple sources in two ways (Fig. 12): (1) by integrating similar types of clinical or 'omics' data from various studies (samples) or groups (horizontal data integration) and (2) by integrating different types of 'omics' or clinical data (features) for the same group of samples (vertical data integration).

Integrated studies can be discussed from the following three perspectives:

1. **Data to be Integrated:** Data to be integrated into a cancer analysis are heterogeneous in types (i.e., environmental, lifestyle clinical and omics Data) and formats or modalities (e.g., text, image). Integration of these data can be categorised into two categories: (i) homogeneous data (e.g., omics or clinical only data) integration and heterogeneous data integration (e.g., clinical and omics data). Fig. 12(a) presents these categories of data integration with examples.
2. **Integration strategy or Levels:** Based on the level of data abstraction, integration levels or strategies can be categorised into 3 (Jendoubi, 2021): (i) Early or Data Level Integration (ELI/DLI) integrates two datasets by concatenating them into a single dataset, (ii) Medium- or Feature-Level Integration (FLI) method first extracts features from the datasets and then integrates them,

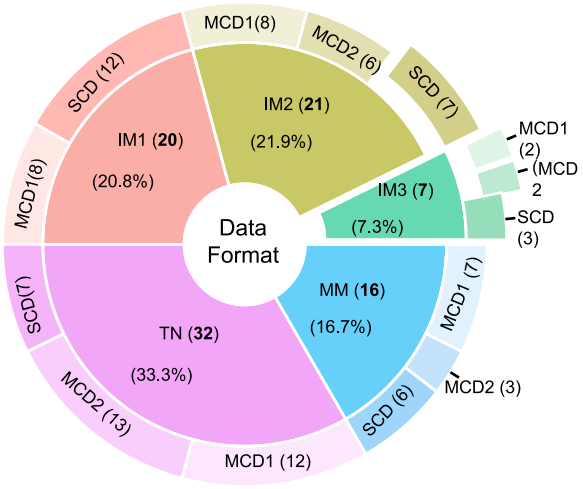

Fig. 11. Data-type (format) and Repository of existing studies (**Acronyms**: IM- Image (1-Radiological, 2-Histopathological, 3-Others), TN- Text or Numeric, MM- multimodal (e.g., image and text), SCD - Single-centred Dataset, MCD- Multi-centred Dataset (1-same country, 2-different countries)).

and (iii) Late or Decision Level Integration (DeLI) method integrates decisions or data models into a high-level model. DLI/ELI can provide higher accuracy at the cost of complexity. On the contrary, DeLI is simpler but less informative than ELI and FLI.

3. **Methods and Tools:** Cancer data integration (DI) methods and tools are diverse (Huang et al., 2017; Zhu et al., 2017; Chakraborty et al., 2018; Wu et al., 2019; Subramanian et al., 2020; Zanfardino et al., 2021), especially for omics data, typically utilising network-based (NB) or Bayesian (BY) approaches or a combination of both. These methods are categorised into four types:

   (a) Network-based non-Bayesian (NB-NBY): These methods use molecular interaction data or build networks based on correlation analysis. Examples include SteinerNet (Tuncbag et al., 2012; Cun and Fröhlich, 2014) and stSVM (Tuncbag et al., 2012; Cun and Fröhlich, 2014), which focus on multi-weighted graphs with multi-omics data.

   (b) Network-based Bayesian (NB-BY): This category relies on Bayesian networks, probabilistic models comprising a graph and a local probability model. Paradigm (Vaske et al., 2010), for instance, integrates multi-omics data using patient-specific pathway activities, while Conexic (Akavia et al., 2010) is another NB-BY algorithm.

   (c) Network-free Bayesian (NF-BY): NF-BY methods can be parametric, "strict" Bayesian, non-parametric, or distribution-free. Parametric methods assume a model for a prior probability distribution, as seen in iCluster (Shen et al., 2009). Non-parametric methods, like MDI (Kirk et al., 2012), do not assume a specific family of probability distributions.

   (d) Network-free non-Bayesian (NF-NBY): These methods do not use NB or BY approaches and may include simple concatenation of datasets. Examples include iPAC (Aure et al., 2013) and CNAmet (Louhimo and Hautaniemi, 2011), designed for specific types of omics data using various approaches.

Integrated Analysis in Existing OC Data Analyses: Figs. 13 and 14, and Table 5 summarise the existing integrated analyses in terms of their key features. In Fig. 13 and Table 5, it is evident that a significant number (32/96) of the studies harnessed integrated data to achieve various objectives. These objectives included disease subtype clustering/classification (Hira et al., 2021), treatment stratification (Laios et al., 2022a), biomarkers prediction (Kim et al., 2021; Bote-Curiel et al., 2022) or treatment efficacy (Laios et al., 2022b), and gaining more information about the biology of OC (Wei et al., 2023). Most of these studies (24/32) integrated homogeneous data (CDI Wei et al., 2023 or ODI Tong et al., 2021); only eight studies considered heterogeneous data or CODI (Liu and Xie, 2021). Two studies (Guo et al., 2020; Hira et al., 2021) of these eight conducted integrated tri-omics analysis without proteomics or metabolomics. For example, the authors of Hira et al. (2021) integrated genomics, epigenomics, and transcriptomics data to cluster and classify OC subtypes. Fig. 13 also illustrates that most (27/32 or 84.4% of the existing studies, including (Guo et al., 2020; Hira et al., 2021), integrated data at the feature level, since the datasets used are readily available with features (e.g., gene expression values, survived months).

On the other hand, Fig. 14, confirms that most studies (84.4% or 27/32)(e.g., Chen et al. (2022) and Wei et al. (2023)) used NF-NBY (NF-NBY1-concatenation, NF-NBY2- correlation and NF-NBY3-ensemble). Only three of the remaining five studies (e.g., Sun et al., 2022; Hao et al., 2019) used NB-NBY, and the other two used the Bayesian approach (NB-BY Ye et al., 2021 and NF-BY Sengupta et al., 2022) approach to integrate their data. One potential reason for most studies (84.4% or 27/32) being NF-NBY-based is the complexity of other methods (Zhu et al., 2017; Chakraborty et al., 2018; Wu et al., 2019; Subramanian et al., 2020).

4.6. Analysis method and existing OC data analyses

Medical data, including cancer data, can be analysed using (Rajula et al., 2020) (i) statistical methods (e.g., linear regression, Cox regression), (ii) ML/DL based methods (e.g., OmiVAE Zhang et al., 2019b), and (iii) hybrid using ML and DL or statistical method and ML/DL (e.g., MMD-VAE4Omics Hira et al., 2021). ML/DL-based analyses offer greater flexibility and scalability than traditional statistical methods, making them suitable for different tasks, including diagnosis, classification, and prognosis. As a result, they might be better suited to advanced big data industries like drug discovery, omics/multi-omics, and personalised medicine. In contrast, conventional statistical methods are more useable when the samples are significantly more than the variables count under study and prior information on the topic under investigation is significant. Although ML/DL-based cancer survival analysis has become available in recent years (e.g., SALMON Huang et al., 2019), combining the two methods would be preferable to one of the methods.

Analysis Methods of Existing OC Data Analyses: We divided the data analysis methods (AM) of the existing studies into (i) DL, (ii) Hybrid1 (DL with ML), and (iii) Hybrid2 (DL with Statistical). As visualised in Fig. 15, most studies (61.45% or 59/96) used DL-based methods to analyse their data, while the rest (38.55% or 37/96) used one of the two hybrid approaches, of which 13.55% (13/96) used Hybrid1 (e.g., OmiVAE Zhang et al., 2019b) and 25% (24/96) used Hybrid2 (e.g., Hira et al., 2021; Hwangbo et al., 2021). One of the reasons most hybrid studies used a combination of DL and statistical methods is that 19 of 96 studies are on prognosis, which generally uses statistical methods, such as Cox regression (Hira et al., 2021). Fig. 15 also highlights that most studies (51/96) used supervised learning (SL) techniques to analyse their OC data.

4.7. ML/DL techniques and algorithms (ML/DLT&A) and existing OC data analyses

There are four ML/DL techniques used in existing cancer data analyses, namely (i) supervised learning (SL), (ii) unsupervised learning (UL), (iii)semi-supervised learning, and (iv) reinforcement learning (RL) (Eckardt et al., 2021). In SL, a labelled training dataset is utilised

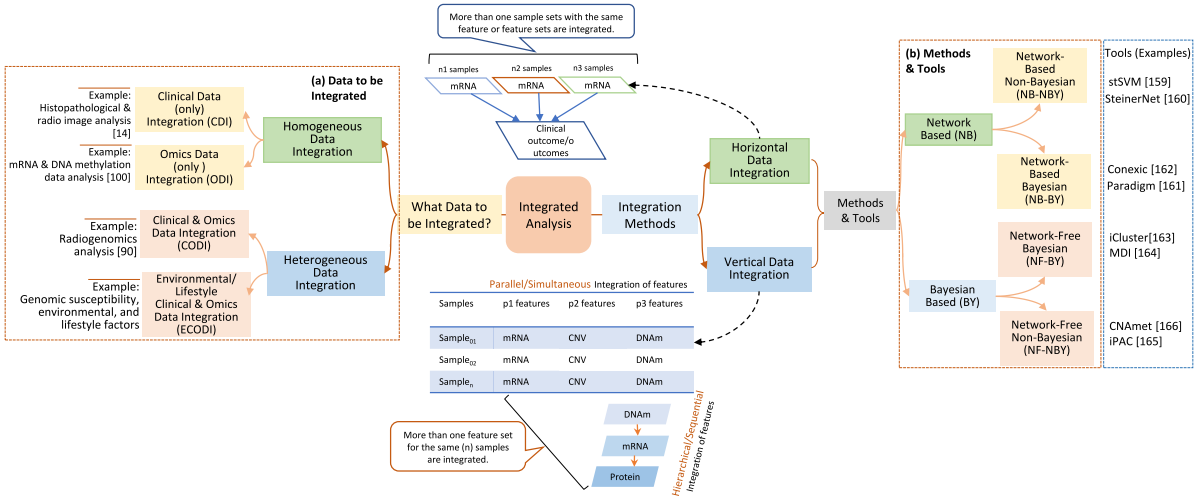

Fig. 12. Data Integration: (a) What data to integrate, and (b) Method & Tools for integration.

Table 5
DL-based integrated data analysis of OC.

Analysis	CSD	CST	Use-of-DA	Data features			Integrated analysis			Analysis Methods & DL details			VM	AIA
				Source	Format	Repository	Data	Level	Method	AM	LT	Algorithms		
Wei et al. (2023)	DD	EOC	C	C	MM	MCD2	CDI	DeLI	NF-NBY3	Hybrid2	SL	CNN	EV2	
Reilly et al. (2022)	DD	OC	C	C	TN	SCD	CDI	FLI	NF-NBY1	DL	SL	MIA3G	IV	
Chen et al. (2022)	DD	OC	C	C	IM1	SCD	CDI	FDeLI	NF-NBY1	DL	SL	CNN	IV	
Sengupta et al. (2022)	DD	OC	C	C	MM	SCD	CDI	DeLI	NF-BY	DL	SL	CNN	IV	
Xie et al. (2021)	DD	OCO	C	C	IM1	SCD	CDI	FLI	NF-NBY1	DL	SL	CNN	IV	
Wang et al. (2021)	DD	OC	C	C	MM	SCD	CDI	DeLI	NF-NBY2	DL	SL	DNN	IV	
Tanabe et al. (2020)	DD	EOC	DQIC	C	TN	SCD	CDI	FLI	NF-NBY1	DL	SL	CNN	IV	
Vázquez et al. (2018)	DD	OC	C	C	TN	MCD1	CDI	FLI	NF-NBY2	Hybrid2	SL	RNN	IV	
Liang et al. (2015)	DD	OCO	SA	CO	TN	MCD2	CDI	FLI	NF-NBY2	DL	UL&SL	DBN	IV	
Ghoniem et al. (2021)	DD	OC	C	CO	MM	MCD1	CODI	DeLI	NF-NBY1	DL	SL	CNN&LSTM	IV	
Chen et al. (2021)	DD	OC	DQIC	CO	TN	SCD	CODI	FLI	NF-NBY1	Hybrid1	UL&SL	GCN	IV	
Sun et al. (2022)	DD	OC	DQIC	O	TN	MCD2	ODI	FLI	NB-NBY	DL	SL	GCN	IV	
Petrovsky et al. (2021)	DD	OCO	C	O	MM	SCD	ODI	FLI	NF-NBY1	DL	SL	CNN	IV	
Ye et al. (2021)	DD	OC	C	O	TN	MCD2	ODI	FLI	NB-BY	DL	UL&SL	GAT&DNN	IV	
Guo et al. (2020)	DD	OC	CCl	O	TN	MCD2	ODI	FLI	NF-NBY1	Hybrid2	UL&SL	AE	EV2	
Mallavarapu et al. (2020)	DD	OCO	Cl	O	TM	MCD1	ODI	FLI	NB-NBY	Hybrid1	UL&SL	RBM&DBN	IV	
Avesani et al. (2022)	DDP	HGSOC	SA	C	IM1	MCD1	CDI	FLI	NF-NBY1	Hybrid2	SL	CNN	EV1	
Hira et al. (2021)	DDP	HGSOC	DQICCl	CO	TM	MCD1	CODI	FLI	NF-NBY2	Hybrid2	UL&SL	VAE&DNN	IV	
Liu et al. (2023)	P	HGSOC	DQISA	C	IM1	SCD	CDI	FLI	NF-NBY2	Hybrid2	SL	CNN	IV	
Zheng et al. (2022)	P	HGSOC	SA	C	MM	SCD	CDI	FLI	NF-NBY1	Hybrid2	SL	RNN	IV	
Wang et al. (2019)	P	OC	SA	C	MM	MCD1	CDI	FLI	NF-NBY1	Hybrid2	SL	DNN	EV1	
Zhu et al. (2021)	P	OC	DQISA	CO	MM	MCD2	CODI	FLI	NF-NBY1	DL	UL&SL	CNN	IV	
Hao et al. (2019)	P	EOC	SA	CO	TN	MCD2	CODI	FLI	NB-NBY	Hybrid2	SL	DNN	IV	
Tong et al. (2021)	P	HGSOC	SA	CO	TN	MCD1	ODI	FLI	NF-NBY1	Hybrid2	UL&SL	AE	IV	
Laios et al. (2022a)	TM	HGSOC	C	C	MM	SCD	CDI	FLI	NF-NBY2	Hybrid1	SL	DNN	IV	
Laios et al. (2022b)	TM	EOC	C	C	TN	SCD	CDI	FLI	NF-NBY1	Hybrid1	SL	DNN&O	IV	XAI
Han et al. (2022)	TM	OC	DQIC	C	IM2	MCD2	CDI	FLI	NF-NBY2	DL	SSL&SL	CNN	IV	
Hwangbo et al. (2021)	TM	HGSOC	C	C	TN	MCD1	CDI	FLI	NF-NBY1	Hybrid2	SL	DNN&O	IV	
Liu and Xie (2021)	TM	OCO	C	CO	TN	MCD2	CODI	FLI	NF-NBY1	DL	UL&SL	CNN	IV	XAI
Yu et al. (2020)	TM	OC	C	CO	MM	MCD1	CODI	FLI	NF-NBY2	DL	SL	CNN	IV	
Lei et al. (2022)	TMP	EOC	DQIC	C	MM	SCD	CDI	FLI	NF-NBY2	Hybrid1	UL&SL	CNN	IV	
Kim et al. (2021)	TMP	EOC	SA	C	TN	SCD	CDI	FLI	NF-NBY1	DL	SL	DNN	IV	
Bote-Curiel et al. (2022)	TMP	OC	DQIC	CO	TN	MCD1	CODI	FLI	NF-NBY1	DL	UL	AE	IV	XAI

Acronyms: CST- Cancer Subtype, AM- Analysis Method, LT- Learning Technique, VM- Validation Method, AIA- AI Assurance, OC- Ovarian Cancer, EOC- Epithelial Ovarian Cancer, HGSOC- High-grade Serous Carcinoma, OCO- OC and others, C- Classification/Clinical, Cl- Clustering, DQI-Data Quality Improvement, DQIC- DQI and Classification, DQICCl-DQIC and Clustering, SA- Survival Analysis, O- Omics, CO- Clinical and Omics, IM- Image (1- Radiological, 2- Histopathological, 3- Others), TN- Text or Numeric, SCD - Single-centred Dataset, MCD-Multi-centred Dataset (1- same country, 2- different countries), CDI- Clinical Data Integration, ODI- Omics Data Integration, CODI- Clinical and ODI, DeLI- Decision Level Integration, FDI- Feature Level Integration, FDeLI- Feature and DeLI, NB-NBY- Network-based non-Bayesian, NF-NBY-Network Free Non Bayesian (1-concatenation, 2- correlation, 3-ensemble), NB-BY- Network-based Bayesian, NF-NB- Network-free Bayesian, Hybrid1- ML and DL, Hybrid2- DL and Statistical, SL- Supervised Learning, UL- Unsupervised Learning, SSL- Semi-Supervised Learning, TL- Transfer Learning, CNN- Convolutional Neural Network, DNN- Deep Neural Network, AE- Autoencoder, VAE- Variational AE, MIA3G- Multivariate Index Assay 3G, RBM- Restricted Boltzmann Machine, LSTM- Long Short-Term Memory, MBiLSTM- Multi-Branch Bidirectional LSTM, GAN- Generative Adversarial Network, GAT- Graph Attention Network, RNN- Recurrent Neural Network, GCN- Graph Convolutional Network, DBN- Deep Belief Network, IV- Internal Validation, EV- External Validation (1- different source but same country, 2- different source and countries), XAI- Explainable AI.

to calculate or map the input data to the preferred output. On the other hand, UL techniques consider only unlabelled training data without assuming a particular output(s) during the learning process. Instead, the learning model finds patterns or groups within the training data. Clustering, dimensionality reduction, and rule-based association learning are the main unsupervised activities, whereas SL techniques mainly perform classifications and regression using linear and non-linear algorithms (e.g., ANN, DL). SL techniques need a large number of labelled

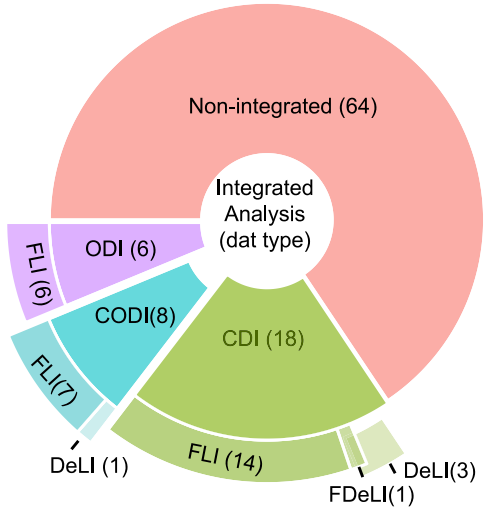

Fig. 13. Data-type (format) and Integration levels (**Acronyms:** CDI- Clinical Data Integration, ODI- Omics Data Integration, CODI- Clinical and ODI, DeLI- Decision Level Integration, FDI- Feature Level Integration, FDeLI- Feature and Decision Level Integration).

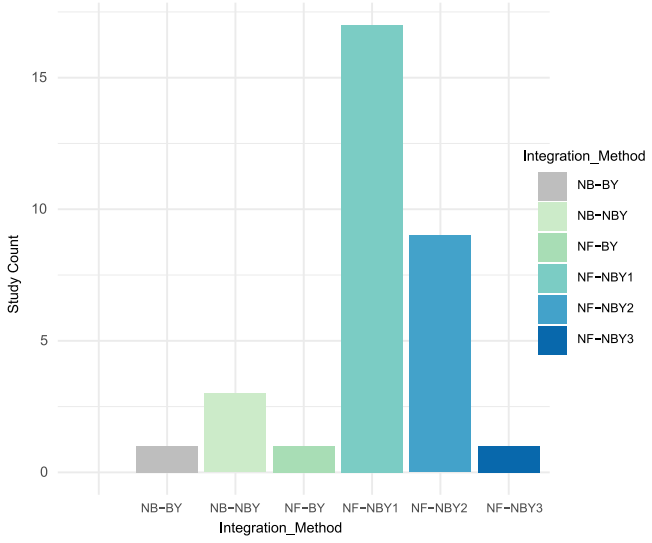

Fig. 14. Integration methods of existing integrated studies (**Acronyms:** NB-NBY-Network-based non-Bayesian, NF-NBY-Network Free Non-Bayesian (1-concatenation, 2- correlation, 3- ensemble), NB-BY- Network-based Bayesian, NF-NB- Network-free Bayesian).

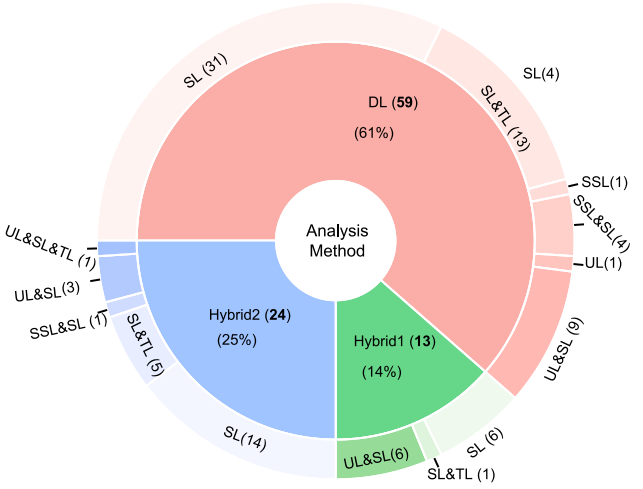

Fig. 15. Analysis methods and learning techniques of existing works (**Acronyms:** Hybrid1- ML and DL, Hybrid2- DL and Statistical, SL- Supervised Learning, UL-Unsupervised Learning, SSL- Semi-Supervised Learning, TL- Transfer Learning).

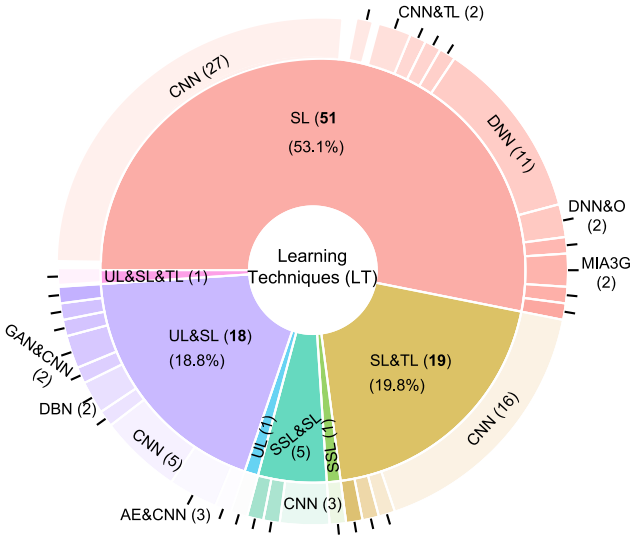

Fig. 16. Learning techniques and algorithms of existing works (**Acronyms:** SL-Supervised Learning, UL- Unsupervised Learning, SSL- Semi-Supervised Learning, TL-Transfer Learning, CNN- Convolutional Neural Network, DNN- Deep Neural Network, AE- Autoencoder, VAE- Variational AE, MIA3G- Multivariate Index Assay 3G, GAN-Generative Adversarial Network).

data to achieve high classification/prediction accuracy. However, the reality is that we often have only a few labelled data and a much more significant amount of unlabelled data in medical domains. Moreover, UL techniques struggle in performance, and transfer learning (TL) techniques need less labelled data than SL, but the number of labelled data required for TL is still quite large (Pocevičiūtė et al., 2021; Khalifa et al., 2019).

Semi-supervised learning (SSL) uses labelled and unlabelled data and is a low-cost alternative to arduous and sometimes unworkable sample labelling. Recently, many cancer-related works have used SSL for classification (Zemmal et al., 2016; Al-Azzam and Shatnawi, 2021) and clustering (Peikari et al., 2018; Ma and Zhang, 2018). SL, UL, and SSL techniques are currently the most popular techniques for cancer data analysis using retrospective data. However, these techniques must better capture the dynamic circumstances in which an individual patient and clinician find themselves during oncological treatment. Since patient and environmental variables change over time, the sequential basis of RL makes it a better fit for capturing the dynamics of oncologic therapy in real-world (prospective) scenarios. Like gameplay and autonomous driving, RL-based ML/DL techniques, which can be value-based, policy-based, and model-based, are also gaining popularity in cancer data analysis (Balaprakash et al., 2019; Daoud et al., 2020).

ML/DLT&A of Existing OC Data Analyses: Fig. 16 presents the distribution of existing studies in terms of ML/DLT&A. In Fig. 16, it is evident that most studies (53.1% or 51/96) used SL techniques, and the rest of the studies used a combination of technologies, including SL&TL (19.8% or 19/96), and UL&SL (18.8% or 18/96). The dominance of SL technique-based studies is due to the availability of labelled data (e.g., TCGA database UCSC, 2020). Similarly, the use of transfer learning (TL) is increasing due to the availability of many pre-trained and reliable models (e.g., ResNet Xie et al., 2021, U-Net González et al., 2021).

Table 6 summarises the main DL algorithms with one or more representative studies used in the existing DL-based OC data analysis.

Table 6
The list of main DL algorithms used in the existing studies.

Algorithm	Description	Examples existing studies
AE/VAE	Neural networks are used for unsupervised learning by compressing and reconstructing data.	Bote-Curiel et al. (2022), Hira et al. (2021), Guo et al. (2020) and Kilicarslan et al. (2020)
CNN	Neural network type using convolutional layers to extract characteristics, mainly in image processing.	Avesani et al. (2022), Tanabe et al. (2020) and EOCSA (2022)
LSTM	A type of recurrent neural network designed to remember information for long periods.	Ghoniem et al. (2021)
MBiLSTM	Enhanced LSTM with multiple branches for bidirectional sequence processing.	Jeya Sundari and Brintha (2023)
TL/Tr	Technique, where a pre-trained model is adapted to a new but related task.	Christiansen et al. (2021), Du et al. (2018) and AlShibli and Mathkour (2019)
DBN	Probabilistic generative models are composed of multiple layers of stochastic latent variables.	Liang et al. (2015) and Mallavarapu et al. (2020)
DCAS	Combines deep convolutional networks with attention mechanisms for survival analysis.	EOCSA (2022)
DeepCox	Integrates deep learning with Cox regression for survival data modelling.	Liu et al. (2022a)
DNN	Traditional deep neural network with multiple hidden layers for feature learning.	Kim et al. (2021) and Hao et al. (2019)
FCN	Network where each neuron is connected to every neuron in the previous layer.	Wang et al. (2023b)
GAN	Consists of a generator and discriminator network, used to generate new data samples.	Levine et al. (2020)
GCN	Neural network that operates on graph data, learning features based on graph structure.	Sun et al. (2022)
MIA3G	Uses the multivariate index assay for genomic data analysis.	Reilly et al. (2022)
RNN	Neural network designed for sequential data processing, maintaining a memory of previous inputs.	Zheng et al. (2022)
1D-CNN	Convolutional neural network applied to one-dimensional data.	Mohammed et al. (2021)
2D-CNN	Convolutional neural network applied to two-dimensional data like images.	Avesani et al. (2022) and Tanabe et al. (2020)
ResNet	Deep neural network using skip connections to prevent the problem of vanishing gradients.	Xie et al. (2021)
U-Net	U-Net is a convolutional neural network or a CNN architecture for semantic segmentation.	González et al. (2021)
Mask-RCN	Extends R-CNN by adding a branch to predict segmentation masks.	Zhu et al. (2021)
MICNN	Convolutional network that processes multiple instances for tasks like object detection.	Jian et al. (2022) and Jian et al. (2021)

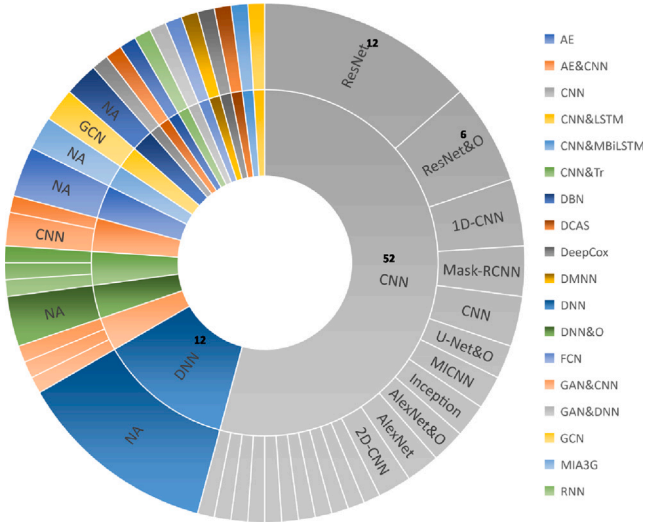

Fig. 17. Distribution of DL algorithms used in existing works (**Acronyms:** AE- Autoencoder, CNN- Convolutional Neural Network, AE & CNN- AE and CNN, LSTM- Long Short Term Memory, MBiLSTM- Multi-Branch Bidirectional LSTM, TL/Tr- Transfer Learning, DBN- Deep Belief Network, DCAS- DeepConvAttentionSurv, DeepCox- Deep Learning and Cox regression, DNN- Deep Neural Network, DNN & O- DNN and Others, FCN- Fully Connected Network, GAN- Generative Adversarial Network, GCN- Graph Convolutional Network, MIA3G- Multivariate Index Assay 3G, RNN- Recurrent Neural Network, 1D-CNN- One dimensional CNN, 2D-CNN- Two dimensional CNN, O- others, ResNet- Residual Network, Mask-RCNN- Mask Region-based CNN, MICNN- Multiple Instance CNN, NA- No specific detail available).

As seen in Fig. 17, CNN is the dominant (52 out of 96) DL algorithm in existing studies (e.g., Avesani et al. (2022), Tanabe et al. (2020) and EOCSA (2022)), and this is mainly due to the prevalence of image-based analysis (48 out of 96 studies). CNN-based algorithms are known to perform better in image data analysis. Furthermore, ResNet is the dominant variant of CNN used in existing ovarian cancer data analyses, with 18 out of 96 studies (34.6%) using it. ResNet's popularity may stem from its use of identity mapping for the residual function (Xie et al., 2021). This method simplifies training by focussing on learning the residual mapping instead of the actual mapping. Another common CNN architecture is U-Net, used by five existing studies, including (Hu et al., 2023; González et al., 2021) mainly for image segmentation.

In addition, most CNN algorithms or architectures (Avesani et al., 2022; Tanabe et al., 2020; EOCSA, 2022)) are 2D-CNN due to the 2D structures of the images used, and four studies (Mohammed et al., 2021; Jeong et al., 2022; Petrovsky et al., 2021; Kopylov et al., 2021) 1D-CNN and two studies (Petrovsky et al., 2021; Jeya Sundari and Brintha, 2023) used 3D CNN to analyse their OC datasets.

In addition, DL-based cancer data compression, DQI, or feature extraction is rising. Seven existing studies, including (Bote-Curiel et al., 2022; Hira et al., 2021; Guo et al., 2020; Kilicarslan et al., 2020), used an autoencoder or a variant of it, including VAE, to compress/reduce the dimensionality of the data set before performing the downstream analysis. One reason for this is their better performance compared to their ML-based counterparts, such as PCA (Zhang et al., 2019b; Hira et al., 2021), and also VAE or its variants are generative DL, which can generate new samples, could be useful where new samples are needed.

4.8. Models Validation Method (VM), and existing OC data analyses

In any data analysis, learnt ML/DL models need to be evaluated through a validation process. Typically, a validation method estimates the accuracy, sensitivity, and specificity of data not seen in the training set. Generally, a validation process can be categorised as "internal" and "external" (Ramspek et al., 2020; Echle et al., 2021). Internal validation (IV) methods are economical and widely used validation methods (VM) that can use one of the three techniques: (i) holdout sample, (ii) cross-validation, and (iii) bootstrapping.

Most cancer data analysis uses IV techniques, but due to possibly biased training data and the complex process, they cannot ensure the quality of an ML/DL model. External validation (EV) is required for the quality of an ML/DL model, such as robustness and generalisability (Siontis et al., 2015; Ho et al., 2020; Echle et al., 2021). Unlike IV, EV uses external or independently emanated datasets to evaluate the performance of a trained model. As a result, EV is often known as independent validation. As the dataset comes from a separate origin, any incorrectly chosen feature set due to quirks in the input training dataset (such as technical or sample bias) would probably fail. As a result, better EV performance can be considered as evidence of generalisability (Ho et al., 2020; Ramspek et al., 2020). We can divide EV into two: EV1-if the test/validation dataset(s) comes from different sources (e.g., clinics/hospitals) but from the same country or demography as the training data, and EV2-if the test/validation dataset(s) come from

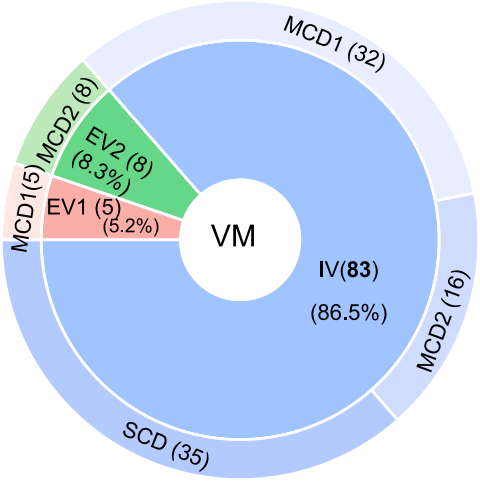

Fig. 18. Validation Methods (VM) and repositories of existing works (**Acronyms:** IV- Internal Validation, EV- External Validation (1- different source but same country, 2- different source and countries, SCD - Single-centred Dataset, MCD- Multi-centred Dataset (1-same country, 2-different countries)).

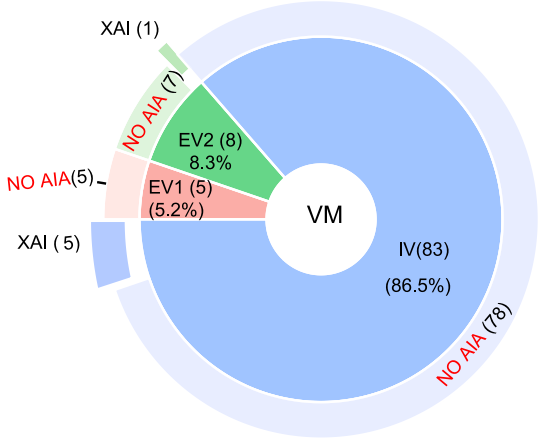

Fig. 19. AIA in existing OC data analyses (**Acronyms:** IV- Internal Validation, EV- External Validation (1- different source but same country, 2- different source and countries, XAI- Explainable AI).

different sources and different country or demography than the training data.

VMs of Existing OC Data Analyses: Fig. 18 illustrates the distribution of the existing OC data analyses in terms of their VM employed. The figure demonstrates that 86.5% (83 out of 96) of the studies utilised IV to validate their DL models. Five of the thirteen studies, including (Avesani et al., 2022; Wang et al., 2019) opted for EV1, while the remaining eight, including (Wei et al., 2023; Guo et al., 2020) chose EV2. Furthermore, the figure highlights a noteworthy pattern in validation practices. All studies that underwent external validation utilised multi-centred (MCD1 or MCD2) datasets. Importantly, studies (Wei et al., 2023; Guo et al., 2020) validated using EV2, did not use test datasets from more than two (Zhao et al., 2020; Shin et al., 2021; White et al., 2022; Guo et al., 2020) demographics. On the contrary, many studies (48 of 83 or 50% of 96 studies) relied on multi-centred datasets for internal validation. This trend might arise from the challenge of obtaining a sufficient volume of samples for training DL algorithms, forcing researchers to employ multi-centred datasets for algorithm training rather than testing purposes.

4.9. AIA principles and existing OC data analyses

AI assurance ensures AI systems' reliability, safety, and trustworthiness, including those used for cancer data analysis. Although AIA principles apply to AI in general, their implementation must consider the specific domain and goals (Batarseh et al., 2021). For OC data analysis using deep learning (DL), some key AIA considerations are:

1. Data quality and bias: One of the most significant challenges in AIA for OC or any cancer data analysis using DL is data quality and bias. Ovarian cancer data, especially medical imaging and omics data, can be complex, heterogeneous, and subject to biases. The dataset must be representative, unbiased, and privacy-preserved to develop fair and trustworthy DL models. AIA should address data provenance, curation, and potential biases to mitigate risks of model failures or unfair outcomes.
2. Interpretability and Explainability are desirable and essential in DL models used for OC or any cancer diagnosis, prognosis, and treatment recommendations. Understanding and explaining the reasoning behind predictions is a crucial factor in gaining the trust of clinicians and patients. Therefore, explainable AI (XAI) techniques tailored to cancer data modalities and clinical workflows are crucial for AIA in this domain. DL models for OC diagnosis should be interpretable and transparent, allowing clinicians to understand the reasoning behind predictions.
3. Safety and robustness: DL models must be rigorously tested and validated to perform reliably and safely without adversarial vulnerabilities or potential patient harm (Department for Science, Innovation & Technology, 2024).
4. Ethical and Social Implications: The use of DL for OC diagnosis should align with ethical principles, such as respecting patient autonomy, beneficence, and non-maleficence (Xu et al., 2022). The use of DL in ovarian cancer care raises ethical concerns related to patient privacy, fairness, and potential biases. AIA should address these issues by incorporating ethical principles, stakeholder engagement, and responsible AI practices specific to cancer.

AIA in Existing OC Data Analyses: AIA is a new but active research area. No study has explicitly addressed AIA with all six goals/aspects in the medical or healthcare domain. As illustrated in Fig. 19, only 6.25% (6/96) of the existing OC data analyses addressed one aspect (XIA) of AIA. All of these 6 studies (White et al., 2022; Laios et al., 2022b; Wang et al., 2023b; Nasimian et al., 2023; Liu and Xie, 2021; Bote-Curiel et al., 2022) evaluated XAI through interpretability. For example, the authors in White et al. (2022) used mones (morphological genes) to interpret CNN-derived image features and cancer phenotypes. On the other hand, the authors in Laios et al. (2022b) demonstrated that XAI using the SHAP (Shapley Additive Explanations) framework can interpret the influence of human factors on the surgical effort for the cytoreductive outcome. However, none of the existing studies used completeness (one of the two ways of evaluating XAI Freeman et al., 2022) to evaluate the explainability of their AI models. Interestingly, 5/6 studies are from the T&M subdomain and only one from the D&D subdomain.

5. Open research challenges and research directions

Despite advances in data analysis using DL in OC, some unresolved research challenges remain to be addressed. For example, further investigation is necessary for predicting and preventing OC, data diversity and DL models' assurance, integrated clinical-multi-omics analysis, and external validation methods. In particular, most (86. 5%, Fig. 18) current studies validated their models internally. In addition, 84. 4% of the existing integrated studies used NF-NBY-based integration methods. Furthermore, only 6. 25% (6/96, Fig. 19) of the studies partially

addressed AIA through XIA or interpretability. In general, although considerable progress has been made in overcoming obstacles to deep learning-based data analysis in cancer, including ovarian cancer, there are still some challenges that need to be addressed.

5.1. Cancer subdomains

Unfortunately, risk prediction for cancer using DL-based data analysis in OC is currently not available. Furthermore, current research has not yet covered the subdomains of TM and prognosis as thoroughly as DD (66/96, Fig. 5), leaving room for significant future advancements in these areas.

5.2. Data features

- Balance Dataset: Imbalanced data distribution and unequal quality in the majority and minority classes of datasets can result in incorrect classification. This imbalanced dataset is a significant concern, as a wrong diagnosis can have fatal consequences for cancer patients. Therefore, while efforts to balance datasets are essential, examining the issue of class imbalance from a medical perspective is equally crucial.
- Sample Size and Diversity: Studies (Benkendorf and Hawkins, 2020) showed that with smaller sample sizes (100–1000), deep learning has no obvious advantage. However, most existing OC data analysis sample sizes are between 20–500. Furthermore, cancer is a multi-factorial disease (Kim and Kim, 2018). Therefore, DL algorithms must be trained on diverse datasets not limited to demography and Behravan et al. (2020) an ethnic group. However, 75% of existing DL-based OC studies (SCD or MCD1, Fig. 13) are limited to a demography or population. Furthermore, only 6% of the remaining 25% studies (Zhao et al., 2020; Shin et al., 2021; White et al., 2022; Guo et al., 2020) considered datasets from two demographics. Therefore, research for robust and clinically acceptable models using large and diverse datasets is necessary.
- Data Quality: Training data quality can significantly improve cancer diagnostic performance (Meng et al., 2021). Sometimes, data quality enhancement, including transformation, may decrease the need for diverse large datasets for generalisable DL models. Many (38 of 96) existing studies used DL techniques to improve data quality, especially image quality. However, with a minimal (2/96) (Hira et al., 2021; Levine et al., 2020) use of generative AI models, further research is needed in this direction.

5.3. Integrated analysis

A significant number (32/96, Fig. 13 and Table 5) of the existing studies performed an integrated analysis of the OC data. Most of these studies considered CDI and only eight were on CODI. Furthermore, only two (Guo et al., 2020; Hira et al., 2021) of these eight studies performed integrated tri-omics analysis without proteomics or metabolomics. Considering the importance of CODI in cancer, more research is needed in this direction, including tetra- and penta-omics analysis (Hira et al., 2021).

5.4. DL techniques and models

Insufficient Data and Transfer Learning: Standard DL algorithms are trained on thousands, if not millions, of human-labelled samples outside of cancer research. Despite the decreasing cost of creating data, including molecular readings using various technologies, access to large amounts of high-quality datasets in precision oncology still needs to be improved. One solution to this challenge is transfer learning (TL). Some existing studies (Tanabe et al., 2020; Christiansen et al., 2021; Du et al., 2018; AlShibli and Mathkour, 2019) used TL. More research must be done using TL to address the issue of data insufficiency in oncology.

Model for Small Data: Model for small data is ongoing in various domains, including cancer (Ko et al., 2021). However, existing DL-based OC studies have yet to explore this. Hence, research is needed on models for small cancer data.

Generative AI in Cancer Research: Deep generative models, one of which type (Large Language Models) has recently revolutionised the world, can be used in health and medical care research (Egli, 2023), including cancer. Only two existing studies used generative models in their analyses. One used a variational autoencoder (a DL-based generative AI algorithm Zhao et al., 2017) for data compression (Hira et al., 2021), and another used GAN for data image generation (Levine et al., 2020). More research is needed to explore the possibility of generating normal/benign samples for relevant cancer.

Hybrid Models and Reinforcement Learning (RL): A combination of ML and DL algorithms or different DL algorithms can improve a DL system's performance by taking advantage of both algorithms. Inspired by this, some OC data analyses (Wang and Zeng, 2021; Sengupta et al., 2022; Hira et al., 2021; Liu et al., 2022b; Kilicarslan et al., 2020) have proposed hybrid (ML and DL) solutions and improved their performance compared to their single algorithm-based counterparts (ML or DL). On the contrary, RL has not been widely studied in cancer research. RLs integrated with DL algorithms (Eckardt et al., 2021) have already made their way to precision oncology but have yet to be used in OC.

5.5. AI assurance

Considering the associated risks of DL in health and medical care, including the assurance of the six aspects of DL systems. However, only 6.25% (6/96) (Fig. 19) of the existing studies addressed an aspect (XIA) of AIA. The other five goals/aspects of AIA, including trustworthiness (critical for healthcare care), have not yet been considered. Most studies used datasets from a population or from a country, which could bias the DL model towards that population. In addition, publicly available databases could be a target of data poisoning (security). So, immediate research is needed on other aspects of AIA, including trustworthy, fair, and secure DL/AI.

5.6. Validation method:

Clinical validation is the biggest obstacle (Echle et al., 2021) in the development of DL systems in health and medical care. Using one dataset to develop and validate a model can lead to overfitting, resulting in a system that only works well for that particular group of patients rather than others. Therefore, validating the DL system with external datasets, preferably from multiple centres, is crucial to ensure that it can be used in routine practice and receive regulatory approval. However, as summarised in Fig. 18, 8. 3% (8/96) of the existing studies performed external validation with multi-centre and multi-country datasets (Zhao et al., 2020; Shin et al., 2021; White et al., 2022; Guo et al., 2020) or data from different populations. Therefore, research with multi-centre and diverse demographic datasets is needed.

6. Summary and future work

ML/DL-based cancer data analysis is necessary for understanding and management of the disease. Many DL-based data analyses have focused on OC. The analyses are diverse in terms of (i) the cancer type they address, (ii) their goals (e.g., prediction, detection), (iii) types and origin/source of the data, (iv) data integration methods and (v) their DL technique utilised for the analyses. To provide a holistic view of these diverse analyses, we present a systematic review of the field, especially from the perspectives of the key features of cancer data analysis and AIA.

The comprehensive analysis of 96 studies revealed a series of key insights that highlight both achievements and gaps in this growing field.

- A predominant emphasis on detection and diagnosis (71% of the studies) subdomain, while regrettably, no endeavours were found to address the subdomains of prediction and prevention of OC.
- noteworthy observation emerged from the geographic confines of the analysed studies, with 75% restricted solely to specific regions or countries, limiting the generalisability of their findings.
- The exploration of integrated analyses was limited (33% of studies), primarily confined to homogeneous datasets such as clinical or omics data.
- Furthermore, only 8.3% of the studies validated their models using diverse and external datasets, highlighting the need for rigorous model validation.
- Incorporation of AIA within the cancer data analysis sphere has emerged as nascent, with only a tiny 5.2% explicitly addressing this crucial aspect through explainability. This highlights the pressing need to embrace AIA comprehensively, encompassing all six goals of AIA, including trustworthiness, fairness, and security.

Based on the findings discussed above, certain research areas need to be focused on to address the identified gaps. These are:

- Exploring diverse and heterogeneous integrated data-driven analyses to uncover novel insights and patterns within complex datasets. The analysis could leverage global sensitivity analysis and deep learning models to handle heterogeneous data sources effectively.
- Robust validation of models through external datasets that span diverse demographic populations ensures the generalisability and robustness of the developed models across different subgroups and minimises potential biases.
- A coordinated emphasis on AI assurance, encompassing all AI goals, such as fairness, transparency, safety, and robustness, to build reliable and trustworthy AI systems that can be deployed in real-world scenarios.

CRediT authorship contribution statement

Muta Tah Hira: Writing – original draft, Resources. **Mohammad A. Razzaque:** Writing – review & editing, Visualization, Methodology, Data curation, Conceptualization. **Mosharraf Sarker:** Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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