Author: Alexandra Makhlysheva (translation from the Norwegian knowledge summary on Federated Learning technology by Alexandra Makhlysheva). Norwegian Centre for E-health Research. 2023.

Federated learning

Healthcare institutions generate and store large amounts of health data. These data have great potential to provide new insights into disease development, increase diagnostic accuracy, and improve treatment outcomes. Collecting, annotating, and maintaining high-quality data takes significant time and human resources. Moreover, access to and/or sharing of health data outside of healthcare institutions is often very limited, among others due to privacy concerns. Health data are considered sensitive personal data and their use is strictly regulated. Anonymizing data is often not enough to protect privacy. For example, it is possible to reconstruct a patient's face from CT, MRI, and PET data (1–3).

Federated learning (4) (FL) is emerging as a promising technique for utilizing distributed data and computational resources while maintaining data security and privacy. However, the technology needs more research to realize its full potential.

What is federated learning?

Federated learning exploits machine learning (ML) methods to *analyze the data where they are stored and avoid them being visible to or shared with external actors*. This makes the technology more privacy friendly.

Healthcare institutions can establish a federated consortium (a decentralized network of organizations) to *train an ML model without exchanging sensitive data with each other*. Each organization can have different roles in the consortium: participate in the model training, validate developed models, or only provide simple queries.

A model training round in a federated consortium can look as follows (Figure 1). First, the latest version of a global model is downloaded by all the organizations in the consortium. Then the model is trained locally in each organization based on local data. Local model updates are then sent to a central server. There, an average of all received local model updates is extracted to improve the global model. The updated global model is then ready to be downloaded by all participants. This process is *iterative* and ends when the model is fully trained.

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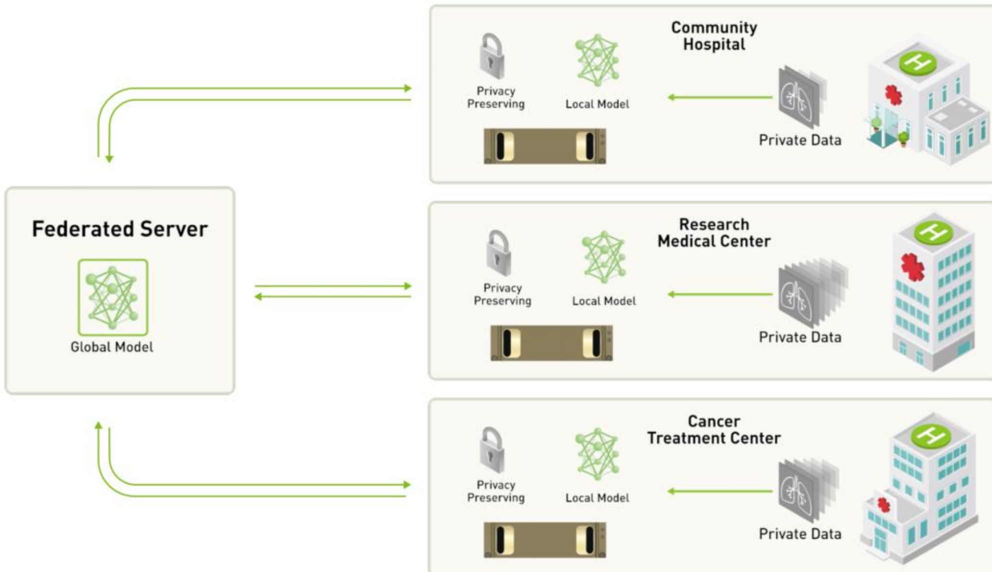

Figure 1: Federated learning with the central server in healthcare. Source (5)

The World Economic Forum has published a guide that describes how a federated consortium for sharing sensitive health data can be established. There they point out the success factors for creating a solid consortium that aims to analyze distributed health data and preserve privacy, data security and integrity (6). When healthcare institutions establish such a consortium, it is a prerequisite that differences in equipment, infrastructure, and data in the organizations as well as how these issues should be handled are considered. Established "ground rules" make it relatively easy to add more healthcare institutions to the federated consortium.

What are the benefits and challenges of federated learning?

When considering the use of federated learning, both the benefits and challenges of the technology must be discussed.

Advantages

Protected privacy, better control over data and reduced risk of data breaches

Federated learning can increase the accuracy and robustness of AI in healthcare and help with large-scale adoption of AI in healthcare (7). Research shows that ML models trained with federated learning can be as good as those trained on centralized data (8). At the same time, federated data are generally less susceptible to attacks than large, centralized databases. The FL approach is also more privacy-friendly because data processing and management of privacy policies and other types of policies are done locally. Hospitals and clinics retain control over patient data by deciding how the data can be used and tracking their use. Patients are then more confident that the data remain within a healthcare institution and that granted data access can be withdrawn. This can make citizens more willing to share their data for research and development.

Larger and more representative data base - better healthcare

Federated learning makes it possible to analyze larger data sets, and therefore the data often becomes more representative. Access to more data across different patient groups and over time enables bigger and better health research studies and more accurate ML-based decision support systems, among others. This can expand clinicians' expertise, ensure more consistent, high-quality clinical decisions, and provide patients with equal quality of care, regardless of location and conditions.

Challenges

Use of resources

Systems using this technology can provide resource savings and lower environmental footprint compared to centralized ML approaches (9). On the other hand, resource usage can increase with undergoing intensive message exchange and the use of several privacy-preserving techniques.

Moreover, participating in a federated consortium also requires an investment in computational infrastructure, especially when participating in the model training process, which is quite costly.

Variations in technical parameters

The storage, computational and communication capacities of organizations can vary (10). An organization may drop out during a training round due to connectivity limitations or insufficient storage capacity. In addition, an organization may decide not to participate in the training round. Therefore, systems using federated learning must have mechanisms to monitor and tolerate (a) a low number of participants in the training process, (b) variations in hardware, and (c) some participants dropping out during the training process.

Variations in data parameters

Data in healthcare institutions can vary considerably in terms of quantity, quality, and data structures. Procedures for checking data quality as well as data standardization and harmonization are important when conducting federated learning (11). Poor quality data (i.e., duplicate, inaccurate, inconsistent, missing, or misspelled data) will lead to biased model results. In a federated consortium, it is difficult to measure a priori the statistical heterogeneity of the training data (i.e., to predict how unevenly health data are distributed across different institutions and to what extent this may affect the outcome). It is also challenging to mitigate the potential negative consequences of this heterogeneity, such as increased complexity in data modeling, analysis, and evaluation (10). There are approaches such as meta-learning (12) and multitask learning (13) which enable the training of multiple local models simultaneously and handle the statistical heterogeneity of the data in a more natural way.

Communication bottlenecks

Federated learning implies intensive message exchange between participating organizations and the central server to communicate model updates. Participants must be resilient to communication failures and delays. It is therefore necessary to implement methods that ensure effective communication and synchronization (14) to (a) reduce the number of communication rounds and (b) reduce the size of the messages in each round.

Potential security threats

There are information security challenges in all systems. Despite the local health data in healthcare institutions are not exposed in systems using federated learning, there is a risk of information leaks from the messages healthcare institutions exchange during model updates. It is therefore a requirement for such systems to have a secure communication system. In a federated consortium of healthcare institutions, participants can be considered trustworthy and intended to follow a certain model training protocol and use their real data for training. However, there is a risk of an intruder taking control of the central server or participating healthcare institutions and attempting to perform various attacks (15).

Attack	Aim	Source of attack	
		Healthcare institutions	The central server
Data and model poisoning attacks	Manipulate local data or a local model to introduce bias into the global model	+	+
Inference attack	Analyze local model updates to gain knowledge about the training process to extract meaningful insights about local data	+	+
Free-ride attack	Uploading fake local updates to obtain the global model without actually participating in the training process	+	-

Here is an overview of mechanisms to strengthen information security and privacy in a federated system (15).

Protection mechanism	What attacks can the mechanism help against?	How does it work?
Differential privacy	• Poisoning attack • Inference attack	Random noise is added to local sensitive data before sharing local model updates with the central server.
Secure multiparty computation	• Inference attack	Local model updates are encrypted before they are sent to the central server. The central server works with the encrypted local model updates.
Anomaly detection	• Free-ride attack • Poisoning attack	Local model updates are analyzed to identify malicious nodes.
Robust aggregation	• Poisoning attack • Inference attack	Before the received local model updates are aggregated on the server (e.g., averaged), malicious local model updates can be

		detected. In addition, the potential contribution of each organization in the training process is measured.
Knowledge distillation	• Inference attack	For more complex models, instead of sharing model parameters, knowledge is transferred from the fully trained complex model to a simpler model (in terms of number of parameters) on what to do to train the simpler model and retain the validity of the model.
Trusted execution environment	• Poisoning attack • Inference attack	A secure area in the processor is used to store the data and execute the training process in each participating organization.
Blockchain	• Poisoning attack • Free-ride attack	All actions and model updates are recorded, tracked, and made visible in blockchain transaction logs.

In federated learning, it is important to ensure the balance between data security and privacy and the performance and accuracy of the trained models. If a distributed system is not secured against attacks, an intruder can manipulate the training process and steal the information. On the other hand, a high level of encryption leads to low model performance, and if too much noise is added to the model updates, the model will have low accuracy.

In other words, the use of federated learning will (a) entail challenges and risks that apply to all distributed systems, (b) require thorough risk assessment and possibly additional security measures, and (c) involve a trade-off between the accuracy of trained models/data analysis and privacy and security.

Federated learning and European data protection regulation

A consortium that performs federated learning in the EU must comply with the GDPR (General Data Protection Regulation). A data controller is responsible for the organization to take the necessary measures to ensure that the system complies with the data protection principles and other requirements of the GDPR. Common challenges in ensuring that a federated consortium complies with the GDPR include defining and sharing responsibilities across multiple data controllers, conducting multiple DPIAs (Data Protection Impact Assessments), conducting audits of participating healthcare institutions and ensuring that the models work as expected.

In the table below, we look at whether it is easier for a system to comply with the data protection principles (16) using FL versus ML on centralized data and whether any measures should be taken.

Privacy principle	Using FL versus ML on centralized data	Description	Possible measures
Fairness, lawfulness, and transparency	When using FL, it is 1) easier to obtain a legal background for	It will be easier to obtain a legal background for data processing since the data are not shared. Organizations have more control over that data	More research is needed. There is a need for tools to check datasets statistical parameters in a distributed and privacy-preserving way, as

	data processing, 2) fairer data processing, and 3) less transparent analysis results.	processing is done with respect for the data subject's interests since data processing is done locally. At the same time, it is more difficult to prove the fairness of decisions, check data sets for bias and statistical heterogeneity since there is no access to the data of the other organizations contributing to the global model.	well as for various visualization tools to improve decision explanation.
Purpose limitation	FL can indirectly facilitate compliance with this principle.	By avoiding centralization and subsequent duplication of data, federated learning can help limit the risk of data being reused for a purpose that is incompatible with the original purpose of data collection.	(Introduce and) follow data governance policies in participating healthcare institutions (i.e., having defined roles, responsibilities, and processes to ensure accountability and ownership of data resources in the organization). The measure will increase local data security.
Data minimization	Better assured with FL	Federated learning avoids the transfer of raw training data to centralized storage and therefore eliminates unnecessary data duplication. It is also easier to ensure that not used anymore data are deleted if they are stored locally.	(Introduce and) follow data governance guidelines in participating healthcare institutions (see Purpose limitation for details).
Accuracy	At best, in line with using ML on centralized data	Local model updates from participants are stored and processed in their original form without any changes and are updated after each training round on the central server, ensuring that the data are always correct. Data from several organizations can be more representative for a population than data from a single organization, resulting in better analysis results. However, models trained with FL are at best as good as those	(Introduce and) follow data governance guidelines in participating healthcare institutions (see Purpose limitation for details). There is also a need for tools to check datasets statistical parameters in a distributed and privacy-preserving way.

		trained on a similar amount of centralized data.	
Storage limitation	Better assured with FL	Neither data from healthcare institutions nor individual local model updates are stored on the central server. It is also easier to ensure that the local data are deleted when training is complete.	(Introduce and) follow data governance guidelines in participating healthcare institutions (see Purpose limitation for details).
Integrity and confidentialit y	Better assured with FL	In federated learning, data are stored locally and not transferred to centralized storage. No individual locally trained model parameters are stored on the central server, only the aggregated results. The global model is stored, but it is anonymous and not considered personal data (17–19).	Various privacy-enhancing mechanisms (e.g., secure multiparty computation, differentiated privacy) can be implemented both on the central server and in participating healthcare institutions, as well as data access control (i.e., rules to control who can access which information or systems), data governance policies (see Purpose limitation for details) and secure communication protocols for a secure message exchange.
Accountabilit y	Better assured with FL	Local data storage provides better control over the data. Simultaneously, the locally stored smaller datasets are of less interest to attacks.	Implement data access control and (introduce and) follow data governance guidelines in participating healthcare institutions (see Purpose limitation for details).

Examples of projects using federated learning in healthcare

There are many studies that have applied federated learning on patient record data to find clinically similar patients (20,21), predict hospitalizations based on cardiac events (22), and the length of stay in the intensive care unit (23). In medical imaging, federated learning is used for whole brain and brain tumor segmentation (8,24,25), pathology (26), and cancer research (27–33). Federated learning has also been utilized to find reliable disease-related biomarkers (34,35), in the context of COVID-19 (36,37), infectious diseases (38), drug discovery (39), workflow analysis (40), and for working with genomic and molecular biology data (41)**Feil! Fant ikke referansekilden.**.

Below is a brief description of health-related projects exploiting federated learning.

International projects

London Medical Imaging & Artificial Intelligence Centre for Value-Based Healthcare (AI4VBH)

AI4VBH (42) is a large project where Kings College London (43), NVIDIA (44) and OWKIN (45) are collaborating to develop a privacy-preserving federated learning system for MRI segmentation of brain tumors (25)**Feil! Fant ikke referansekilden.**. They will connect four teaching hospitals in London before expanding to the whole of the UK. The ambition is to provide artificial intelligence services in a wide range of therapeutic areas, including cancer, heart failure, and brain disease. This is an ongoing project.

Collaboration between Moorfields Eye Hospital and Bitfount on eye disease-related biomarkers

Bitfount (46) collaborates with researchers from Moorfields Eye Hospital (47) in London and the University of Surrey to use federated learning to evaluate biomarker models that can predict certain eye conditions (34). These models flag patients for recruitment to clinical trials, without affecting privacy and reducing recruitment costs. This is an ongoing project.

Bigpicture

Bigpicture (26) is a European public-private partnership of academic institutions, SMEs, public organizations, and pharmaceutical companies, among others, in the field of pathology research. They provide a GDPR-compliant infrastructure (both hardware and software) to store, share, and process pathology images. This is an ongoing project that lasts until 2027.

HealthChain

HealthChain (27) was a French consortium of hospitals, universities, and technology partners for clinical research. They trained ML models on histological and dermoscopic images to predict treatment response for patients with breast cancer and melanoma. The project was completed in 2021.

Melloddy (Machine Learning Ledger Orchestration for Drug Discovery)

MELLODDY (39) was a European consortium of pharmaceutical, technological, and academic partners that applied federated learning to the data from pharmaceutical companies to increase efficiency in drug discovery. The project lasted 3 years and was completed in 2022.

Federated Tumor Segmentation (FeTS)

FeTS (28) is an ongoing international consortium of healthcare institutions and a platform for tumor boundary recognition in MRI images from large and diverse patient populations.

Trustworthy Federated Data Analytics (TFDA)

TFDA (29) is an ongoing German project in cancer research that uses federated learning, with radiation therapy as a use case.

Joint Imaging Platform

Joint Imaging Platform (30) is an ongoing strategic initiative within the German Cancer Consortium that aims to establish a technical infrastructure for distributed medical imaging research.

OPTIMA (Optimal Treatment for Patients with Solid Tumors in Europe Through Artificial intelligence)

OPTIMA (31) is an ongoing European project and platform that will promote cancer treatments and easier decision-making for doctors and patients with prostate, breast, and lung cancer. The platform will be GDPR compliant.

Epiverse

Epiverse (38) is a global collaboration between academia, governments and other organizations developing a reliable data analysis ecosystem of standardized epidemiological software tools for infectious diseases. The project is ongoing and supported by the Rockefeller Foundation (48) and the Wellcome Trust (49).

Projects with Norway's participation

HealthData@EU

This is a 2-year pilot project (ends in 2024) that aims to promote secure access to and exchange of health data across national borders in the EU (50,51) in the European Health Data Space (EHDS). According to the European Commission (52), EHDS will comply with the GDPR, the Data Protection Act (53), the Data Management Act (54), and the NIS2 Directive on cyber security (55); this will promote privacy and data security for European health data. Norway is participating in three use cases, in addition to participating in most of the other work packages in the pilot. One use case is about comparing medical events logs to evaluate interoperability of health data across the EU within cardiovascular and metabolic diseases. The goal is to 1) assess the degree of agreement in data, codes, and standards, 2) study the prevalence of cardiovascular and metabolic diseases across the EU, and 3) develop and validate new and improved prediction models for cardiovascular and metabolic diseases. France, leading this use case, will develop an AI prediction model. Then, in an iterative process, the model will be tested on Finnish, Danish, Hungarian, and Norwegian data and re-calibrated/re-trained. This use case will test the readiness for secondary use of health data across Europe for research, policy making, regulatory activities, and innovation and the maturity of using ML on distributed health data. They seek to gain knowledge and get necessary experience to increase the likelihood of appropriate further use of AI on Big Data.

FederatedHealth: A Nordic Federated Health Data Network

FederatedHealth (56) is an ongoing 3-years project funded by Nordic Innovation, working with clinical notes in electronic health records in Nordic countries (Finland, Sweden, Denmark, Estonia, and Norway). They will use federated learning to develop a privacy-preserving virtual infrastructure for data analysis and research purposes. The infrastructure will be tested on two use cases: 1) detecting medical implants before MRI scans and 2) identifying drug side effects. The knowledge and experience from this project can be further utilized in work processes in EHDS.

Elixir

Elixir (41) is a European project and framework for secure submission, archiving, sharing and analysis of genomic and molecular biology data. The University of Oslo operates the Norwegian part of the EGA network (European Genome-phenome Archive) (57).

Cancer research collaboration with the Netherlands

The Cancer Registry of Norway collaborated with the Cancer Registry of the Netherlands to compare indicators for different patient groups with breast cancer, without exchanging patient information (32).

FLORENCE

FLORENCE (33) (Federated learning using OMOP modelling of health data for elevating colorectal cancer care in the Nordic countries) is a 3-years interregional project that develops a decision-making tool for colorectal cancer clinicians. This is a collaboration between the Cancer Registry of Norway, the Center for Surgical Science (CSS) at Zealand University Hospital in Denmark, Lund University in Sweden, Computerome at the Technical University of Denmark, and the unit for research projects at Zealand University Hospital. They use hospital and registry data harmonized to the OMOP data model to share model changes instead of health data and at the same time have an equally good decision-making tool at all participating institutions. OMOP stands for Observational Medical Outcomes Partnership and is designed to standardize data into a common format (58). The project is funded by Interreg Øresund-Kattegat-Skagerak (ØKS) until 2025.

Workflow-integrated machine learning (WIML)

WIML (40) promotes the development of a research information system, is operated by the Mohn Medical Imaging and Visualization Centre in Bergen, and provides infrastructure for research projects that collect data in hospital systems (both images and structured numerical data are taken for analysis).

PraksisNett

PraksisNett (21) is a research network in the primary health service and an infrastructure that enables distributed analyses from patient records in Norwegian GP offices.

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Conclusion

Federated learning is a privacy-enhancing approach to using machine learning methods for distributed data analysis where several organizations collaborate on model training, while ensuring that the data remains private and inaccessible to external parties. By using machine learning methods in a privacy-preserving way, the technology provides opportunities to harness the potential of large amounts of data in healthcare institutions to provide a better knowledge base for medical decisions and, consequently, contribute to better patient care. There are many ongoing health-related projects using the technology with promising results. However, healthcare institutions contemplating the use of federated learning should consider the following issues: variations in data and technical parameters in organizations, resource use, potential communication bottlenecks, and data security. There is a need for more research before the technology can be fully utilized. There should be developed privacy-preserving methods to check statistical parameters on distributed datasets in the healthcare institutions involved in the training process. Due to the sensitivity and high value of health data, further development of effective cryptographic and privacy-preserving techniques for extra security measures in federated consortia of healthcare institutions is necessary. Moreover, further research is required on the trade-off between privacy and accuracy in data analysis performed in FL systems.

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