Are Population Graphs Really as Powerful as Believed?

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Abstract

Population graphs and their use in combination with graph neural networks (GNNs) have demonstrated promising results for multi-modal medical data integration and improving disease diagnosis and prognosis. Several different methods for constructing these graphs and advanced graph learning techniques have been applied and established to maximise the predictive power of GNNs on population graphs. However, in this work, we raise the question of whether existing methods are really strong enough by showing that simple baseline methods –such as random forests or linear regressions–, perform on par with advanced graph learning models on several population graph datasets for a variety of different clinical applications, such as age regression or disease prediction. We utilise benchmark citation datasets as well as the commonly used public population graph datasets TADPOLE and ABIDE, a brain age estimation and a cardiac dataset from the UK Biobank, and a real-world in-house COVID dataset. We investigate (a) the utility of GNNs for multi-modal data integration in the context of population graphs and (b) the impact of the graph structure on GNN performance. We conclude that GNNs are only beneficial for population graph studies if the graph structure adds meaningful additional information to the node features and show that the node features dominate the predictive power of GNNs in these studies.[1]

1 Introduction

Graphs can be used to model and represent various types of data. They allow for a suitable representation of interconnected structures, such as social networks (Fan et al., 2019), molecules (Moreira-Filho et al., 2022), or surface meshes (Mueller et al., 2023b). In order to perform deep learning on graph-like data structures, graph neural networks (GNNs) have been introduced (Gori et al., 2005; Scarselli et al., 2008). GNNs follow a message-passing scheme and collect information that is stored in nodes across a graph structure (Bronstein et al., 2017) and have shown improved performance of various deep learning tasks (Parisot et al., 2017; Ahmedt-Aristizabal et al., 2021; Bessadok et al., 2022; Pellegrini et al., 2022). Most of these tasks rely on datasets that inherently provide a graph structure, such as social networks, or provide well-established methods to construct the graph, such as point clouds (Wang et al., 2019).

In the medical domain, GNNs have been applied to improve disease diagnostics (Parisot et al., 2017; Cosmo et al., 2020; Kazi et al., 2022), model biological structures (Chen et al., 2020), or temporal components of data (Kim et al., 2021). They can be used to perform deep learning on surface meshes for fatty tissue quantification (Mueller et al., 2023b), vessel structures (Paetzold et al., 2021) for vessel segmentation, or molecules for drug discovery (Bonner et al., 2022). The respective datasets provide an inherent graph structure in the form of a mesh, a vessel tree, or chemical bindings. In contrast to datasets that provide a clear graph structure, some works study so-called *population graphs*. A population graph refers to a network of inter-connected subjects encoding the medical information of all subjects in graph form. Usually, the subjects' medical data, such as imaging or clinical features, is used as node features in the graph and the edges are constructed in a way that similar subjects are connected with each other. Figure 1 shows a schematic of a typical population graph. Each subject considered as a node is represented by a data vector, which is usually extracted from medical images. Additionally, non-imaging clinical data, such as demographics or lab results, can be used to define the edges between subjects.

[1]The source code for this work can be found at: `https://anonymous.4open.science/r/population_graphs`

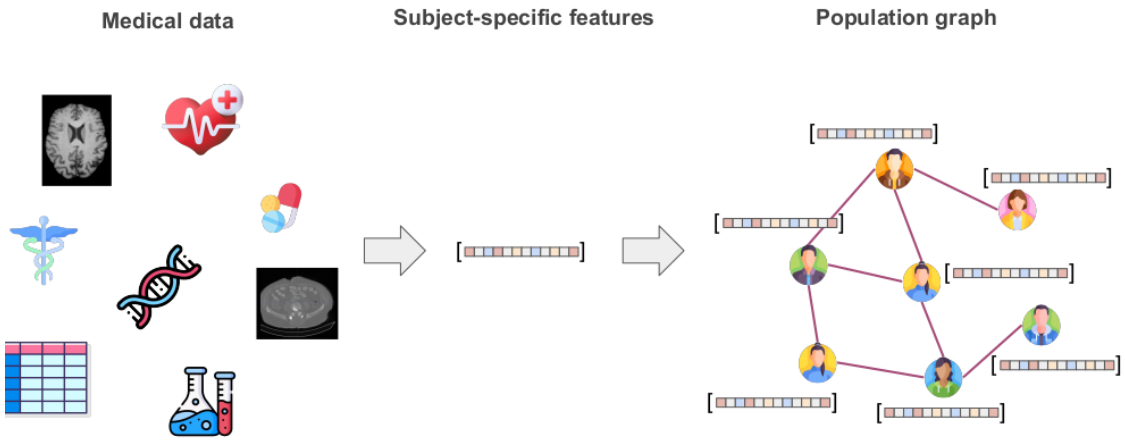


Figure 1: Overview of a typical population graph and its construction. Medical data is represented in the form of a feature vector for each subject and saved as node features in the population graph. The most frequently used setup uses imaging features as node features and non-imaging features for edge construction.

Several works have shown that population graphs for medical applications can improve downstream tasks compared to graph-agnostic methods (Parisot et al., 2017; Kazi et al., 2019; Cosmo et al., 2020; Kazi et al., 2022). However, population graphs come with a significant limitation: the graph structure needs to be constructed from the dataset. This has led to different graph construction methods. Two branches of graph construction have been established: static and dynamic graph construction. Static graph construction refers to the creation of the graph structure prior to graph learning, while dynamic graph construction methods adapt the graph structure during training (Cosmo et al., 2020). To date, both methods are used frequently. What makes the choice of graph construction method so crucial, is the impact of the resulting graph structure on the downstream performance of the GNN. It has been shown that a "poor" graph structure can lead to GNNs under-performing graph-agnostic models (Luan et al., 2022; Zhu et al., 2020). Some methods have been specifically designed to work on such challenging graph structures, one of them being neural sheaf diffusion models (Hansen & Gebhart, 2020). We investigate their potential on population graph datasets, which tend to have challenging graph structures.

So far, there are two commonly used arguments for using medical population graphs compared to graph-agnostic models: (1) GNNs allow for meaningful multi-modal data integration, and (2) the message passing across neighbourhoods improves model performance. In this work, we investigate how firm those claims are and contradict those claims on several datasets. Our contributions can be summarised as follows:

- We compare static and dynamic state-of-the-art graph construction methods with GNNs, as well as the usage of neural sheaf diffusion models for population graphs and show how simple graph-agnostic baselines perform on par with them on several benchmark and population graph datasets.
- We show that GNNs can be superior to graph-agnostic models if the graph structure is provided with the dataset but do not achieve performance boosts on the medical population graph datasets used in this work. We hypothesise that in the latter case, the graph structure does not add additional valuable information.
- We evaluate the impact of the graph structure on several different types of graph convolution, using two different graph assessment metrics: homophily and cross-class neighbourhood similarity (CCNS) distance.
- We discuss the question of whether population graph modelling techniques with GNNs are actually beneficial compared to graph-agnostic methods.

Our results lead us to conclude that we need a discussion about whether population graphs are beneficial over graph-agnostic methods and that the currently available graph construction methods are the performance bottleneck of GNNs on population graphs. We see a requirement for "better" graph construction methods if we want to improve the performance of GNNs on population graphs.

2 Background

In this section, we give some background on graphs, graph neural networks with different graph convolutions, neural sheaf diffusion models, and two graph assessment metrics, namely homophily and cross-class neighbourhood similarity.

2.1 Graph Structures

A graph $G := (V, E)$ is defined as a set of n vertices/nodes V and a set of edges E, where $e_{ij} = 1$ and $e_{ij} \in E$ if there exists an edge from node i to node j. All edges can be summarised in an $n \times n$ adjacency matrix $\mathbf{A}$, where $a_{ij} = 1$ if $e_{ij} \in E$ and 0 otherwise. In the context of graph deep learning, the graph's nodes usually hold node features of dimension r, that can be summarised in the node feature matrix $\mathbf{X} \in \mathbb{R}^{n \times r}$. A neighbourhood of a node i, $\mathcal{N}_i$ is the set of all nodes j, for which there exists an edge e_{ji} from j to i. Furthermore, in the setting of node classification, each node i usually holds a label y_i, and all labels can be summarised in the label vector Y.

2.2 Graph Assessment Metrics

Several works have shown that the graph structure can have a significant impact on the performance of GNNs (Luan et al., 2022; Zhu et al., 2020). In this line, different metrics have been introduced that assess graph structures and have been shown to correlate with GNN performance. The metric most commonly used is *homophily*. One can distinguish between three different types of homophily: class homophily (Lim et al., 2021; Luan et al., 2021), edge homophily (Kim & Oh, 2022), and node homophily (Pei et al., 2020), which all highlight slightly different aspects of the graph structure. They all evaluate the ratio between edges that connect nodes with the same label and edges that connect nodes with different labels. The idea is that since GNNs propagate node features across edges, the less similar the neighbours are, the less likely it is for the GNN to learn representative node feature embeddings for this node, which can impact the network's performance. In the remaining parts of this work, we will use node homophily.

Definition 2.1 (Node homophily (Pei et al., 2020)) *A graph $G := (V, E)$ with node labels $Y := \{y_u; u \in V\}$ has the following node homophily:*

$$\hom(G, Y) := \frac{1}{|V|} \sum_{v \in V} \frac{|\{u | u \in \mathcal{N}_v, Y_u = Y_v\}|}{|\mathcal{N}_v|}, \tag{1}$$

where $\mathcal{N}_v$ is the set of neighbouring nodes of v and $|\cdot|$ the cardinality of a set.

We speak of "high homophily" or a "homophilic" graph, when $\hom(G, Y) \to 1$ and of "low homophily" or a "heterophilic" graph, when $\hom(G, Y) \to 0$. A graph's homophily can also be defined for regression tasks by taking the distance between node feature labels among neighbourhoods into account (Mueller et al., 2023a):

Definition 2.2 (Homophily for regression (Mueller et al., 2023a)) *The node homophily of a graph G with labels Y (defined as above) that indicate a regression task is defined as follows:*

$$\hom_{\text{reg}}(G, Y) := 1 - \left(\frac{1}{|V|} \sum_{v \in V} \left(\frac{1}{|\mathcal{N}_v|} \sum_{n \in \mathcal{N}_v} \|y_v - y_n\|_1 \right) \right), \tag{2}$$

where $\|\cdot\|_1$ indicates the L_1 norm.

Another metric, that does not only focus on the ratio of edges connecting same-labelled or differently-labelled nodes, is cross-class neighbourhood similarity (CCNS) (Ma et al., 2021). Here, the overall similarity of neighbourhoods of nodes with the same label is evaluated, irrespective of whether the neighbours share the same label as the node of interest.

Definition 2.3 (Cross-class neighbourhood similarity (Ma et al., 2021)) *Let $G := (V, E)$, Y, and $\mathcal{N}_v$ be defined as above. In addition, let C be the set of all possible classes of node labels, and V_c the set of vertices of a specific class c. Then the CCNS of two classes c_r and c_s can be derived as follows:*

$$\mathrm{CCNS}(c_r, c_s) = \frac{1}{|V_{c_r}||V_{c_s}|} \sum_{u,v \in V} \mathrm{cossim}(d(u), d(v)), \tag{3}$$

where $d(v)$ indicates the histogram of a node v's neighbours' labels and $\mathrm{cossim}(\cdot, \cdot)$ the cosine similarity.

We note that in this work, we only utilise a dynamic graph learning pipeline, that reduces the continuous adjacency matrix back to a static one by sampling (Kazi et al., 2022). However, both metrics can be extended to continuous adjacency matrices, if other dynamic graph construction methods are used (Mueller et al., 2023a). This allows an evaluation of these graph assessment metrics also in the case of dynamic graph learning, which requires a continuous adjacency matrix. Mueller et al. (2023a) also introduce a reduction of CCNS to a single-valued parameter, they call *CCNS distance*, which defines the L_1 distance between the CCNS matrix and the identity matrix:

Definition 2.4 (CCNS distance (Mueller et al., 2023a)) *Let $G := (V, E)$, C, and* CCNS *be defined as above. Then the CCNS distance of the whole graph G is:*

$$D_{\mathrm{CCNS}} := \frac{1}{n} \sum \|\mathrm{CCNS} - \mathbb{I}\|_1, \tag{4}$$

where $\|\cdot\|_1$ is the L_1 norm and $\mathbb{I}$ the identity matrix.

2.3 Graph Neural Networks

GNNs have been introduced with the aim of enabling deep learning on non-Euclidean spaces, such as graphs, manifolds, or meshes (Bronstein et al., 2017). They all follow a so-called message-passing scheme, which propagates the information, that is stored in the node features of the graph (or mesh or manifold) to its neighbouring nodes. The GNN then learns a node feature embedding, based on the original node features as well as the propagated node features of the neighbouring nodes. GNNs make use of graph convolutions, which specify the concrete message-passing scheme that is applied during training and inference. There exist several different types of graph convolution, all varying slightly in their methodology. We here summarise the definitions of four commonly used graph convolutions.

Definition 2.5 (Graph Convolutional Networks (GCN) (Kipf & Welling, 2016)) *Graph convolutional networks (GCNs) were one of the first GNNs introduced by Kipf & Welling (2016). They were originally defined in a spectral manner, using the graph Laplacian. The* `PyTorch Geometric` *implementation follows the following definition:*

$$x'_i = \Theta^T \sum_{j \in \mathcal{N}_i \cup \{i\}} \frac{1}{\sqrt{\hat{d}_j \hat{d}_i}} \, x_j, \tag{5}$$

where $\hat{d}_i = 1 + \sum_{j \in \mathcal{N}_i} 1$.

Definition 2.6 (Graph SAGE (Hamilton et al., 2017)) *In 2017, Hamilton et al. (2017) introduced a novel graph convolution that was originally designed for large graphs and inductive training, which is called GraphSAGE. Here, the new feature representation of a node i is defined as follows:*

$$x'_i = W_1 x_i + W_2 \cdot \mathbb{E}_{j \in \mathcal{N}_i} \tag{6}$$

Definition 2.7 (Higher-order Graph Neural Networks (GraphCONV) (Morris et al., 2019)) *Morris et al. (2019) introduced so-called higher-order GNNs, where the node feature embedding x'_i of node i is defined as follows:*

$$x'_i = W_1 x_i + W_2 \sum_{j \in \mathcal{N}_i} x_j. \tag{7}$$

Definition 2.8 (Graph Attention Networks (GAT) (Veličković et al., 2017)) *Veličković et al. (2017) introduced a graph neural network, that learns attention weights for edges in the graph. The new node feature embedding of a node i is defined as:*

$$x'_i = \alpha_{ii} \Theta x_i + \sum_{j \in \mathcal{N}_i} \alpha_{ij} \Theta x_j, \tag{8}$$

where α_{ij} is the attention coefficient between two nodes i and j and is defined as follows:

$$\alpha_{ij} = \frac{\exp\left(\phi\left(a^T\left(\Theta x_i \parallel \Theta x_j\right)\right)\right)}{\sum_{k \in \mathcal{N}_i \cup i} \exp\left(\phi\left(a^T\left(\Theta x_i \parallel \Theta x_k\right)\right)\right)}, \tag{9}$$

where ϕ is commonly the LeakyReLU function and $\parallel$ indicates a concatenation of the values.

2.4 Neural Sheaf Diffusion Models

With a rising discussion on how GNNs perform on low-homophily graph structures, different approaches to graph learning have been established that target these more challenging settings for graph learning. One of these methods is neural sheaf diffusion models, originally introduced by Hansen & Gebhart (2020) and extended by Bodnar et al. (2022). They use the topological concept of cellular sheaves, which assign vector spaces to all nodes and edges and linear mappings between them for all node-edge connections. Traditional GNNs are designed in a way that they assume a graph structure with a trivial underlying sheaf. Hansen & Gebhart (2020) and Bodnar et al. (2022) introduce an alternative approach to graph deep learning that is based on the concept of cellular sheaves, where different sheaf representations are learned for nodes and edges of the graph. They show that with this method, they can provide a graph learning technique that is less impacted by heterophilic graphs and over-smoothing - two commonly known limitations of GNNs. Sheaf neural networks (Hansen & Gebhart, 2020; Bodnar et al., 2022) are a generalisation of GCNs (Kipf & Welling, 2016) and leverage the sheaf Laplacian (Hansen & Ghrist, 2019), an extension of the graph Laplacian. This allows for an expression of more complex relationships between nodes rather than "similarity". Bodnar et al. (2022) furthermore show how these sheaves can be learned from the data at hand, using neural networks.

Definition 2.9 (Sheaf Convolution) *Let $\mathcal{F}$ be a sheaf on a graph G with feature matrix $X \in \mathbb{R}^{nd \times a}$ and sheaf lapacian $\Delta_{\mathcal{F}}$. A sheaf convolutional model is then defined as follows:*

$$Y = \sigma\left(\left(I_{nd} - \Delta_{\mathcal{F}}\right)\left(I_n \otimes W_1\right) X W_2\right), \tag{10}$$

where σ is a non-linearity, $\otimes$ denotes the Kronecker product, $W_1 \in \mathbb{R}^{d \times d}$ and $W_2 \in \mathbb{R}^{a \times b}$ are two weight matrices, and a and b define the number of input and output channels, respectively.

The authors introduce different versions of neural sheaf networks, such as *GeneralSheaf*, *BundleSheaf*, and *DiagSheaf*. For more details about sheaf networks, we refer to Hansen & Gebhart (2020) and Bodnar et al. (2022). In this work, we utilise neural sheaf diffusion models on all classification datasets in order to investigate their potential on potentially low-homophily graph structures of medical population graphs.

3 Related Work

In general GNN research, several works have investigated the impact of the graph structure on model performance. Zhu et al. (2020) address the issue of the impact of the graph structure, measured by homophily (see Section 2.2), on different graph convolutional networks on citation networks. Several metrics have been

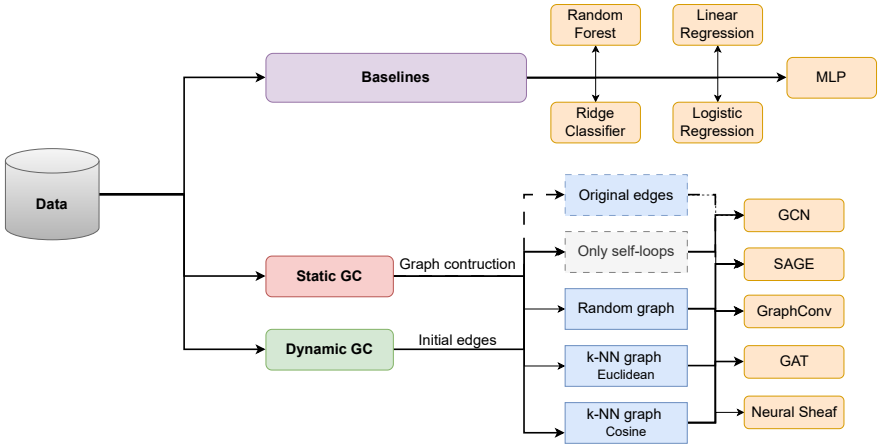


Figure 2: Overview of the conducted experiments. We tune different baselines. We perform static or dynamic graph construction, then pick one of the blue methods (second column) to construct either the static graph structure or the initial edges for the dynamic graph construction pipeline. We then use four different graph convolutions: GCN, SAGE, GraphConv, and GAT, or Neural Sheaf Diffusion Models. The original edges are only used if available.

established, that allow for an assessment of the graph structure and show correlation with the performance of GNNs. Luan et al. (2022) introduce two metrics called normalised total variation and normalised smoothness value, that measure the effect of edge bias. Xie et al. (2020) measure the graph structure with two metrics called neighbourhood entropy and centre-neighbourhood similarity. Ma et al. (2021) utilise the above-mentioned metric called cross-class neighbourhood similarity, which assesses how similar all neighbourhoods of all nodes with the same label are and show their correlation with GNN performance. Most of these works assess their metrics on benchmark datasets, such as citation networks, that come with a ground truth graph structure. In this work, we want to take these experiments one step further and investigate the impact of graph construction methods on population graph studies with GNNs and investigate the benefit of using GNNs over baseline methods.

There is little work investigating the impact of different graph construction methods and different graph learning schemes on the performance of population graphs. Bintsi et al. (2023b), for instance, evaluate different static graph construction methods on an age regression dataset, but do not evaluate dynamic graph construction methods. To the best of our knowledge, this is the first work specifically addressing the challenge of graph construction in population graph studies in combination with different graph learning methods and with a detailed comparison to baseline models.

4 Methods and Training Setup

In this section, we provide an overview of the utilised methods for this work. We introduce the different static and dynamic graph construction methods, summarise the utilised GNN models and the training setup, and introduce the datasets that were used to perform the experiments. A summary of the different learning and graph construction pipelines is visualised in Figure 2.

4.1 Datasets

We perform our experiments on three benchmark classification datasets: CORA, CITESEER, PUBMED (Yang et al., 2016), and five medical population graph datasets: TADPOLE (Yu et al., 2020), ABIDE (Di Martino et al., 2014), a cardiac dataset from the UKBB (Sudlow et al., 2015), and an in-house dataset of COVID patients for classification and a brain age dataset also extracted from the UKBB for a regression task. An overview of the datasets is summarised in Table 1.

Table 1: Overview of all utilised datasets with the respective number of nodes, number of samples/nodes in the train, test, and validation sets, the number of node features (Nr. features), and the number of classes.

Dataset	Nr. nodes	Train samples	Val. samples	Test samples	Nr. features	Nr. classes
CORA	2708	1708	500	500	1433	7
CITESEER	3327	2327	500	500	3703	6
PUBMED	19717	18717	500	500	500	3
TADPOLE	564	468	48	57	30	3
ABIDE	871	609	41	221	6105	2
UKBB Cardiac	2900	2320	58	522	89	2
COVID	65	45	4	16	29	2
UKBB Brain Age	6406	4811	1276	319	88	Regression

CORA, CITESEER, PUBMED In order to evaluate the impact of the graph construction method and the resulting graph structure on the performance of the GNN, we utilise commonly used benchmark citation datasets CORA (2 708 nodes), CITESEER (3 327 nodes), and PUBMED (19 717 nodes) (Yang et al., 2016). These datasets come with a pre-defined graph structure, which we can use as the ground truth graph. We compare the model performance on the ground truth graph structure to the performance on graphs that were generated with different graph construction methods. All datasets are classification datasets.

TADPOLE We use the commonly used subset of the TADPOLE dataset (Yu et al., 2020) that is for example used in Kazi et al. (2022). The task of this dataset is to distinguish between patients with Alzheimer's disease (AD), ones with mild cognitive impairment (MCI), and healthy control groups (NC). The dataset consists of 30 imaging features of 564 subjects.

ABIDE A second public and frequently used dataset for population graph studies is the Autism Brain Imaging Data Exchange (ABIDE) dataset (Di Martino et al., 2014). It contains brain imaging features and clinical features such as age of 871 subjects and has been used in the context of population graphs in several works (Parisot et al., 2017; Kazi et al., 2019; 2022). The task of this dataset is a binary classification task, discriminating between autism patients and healthy controls.

COVID We use a small real-world medical dataset of CoViD patients, that has also been used before in population graph settings (Keicher et al., 2021), however in a slightly different version of the dataset. The task is a binary classification of whether a subject is predicted to require intensive care or not. The dataset consists of image-derived features and clinical features of 65 subjects.

UKBB Brain Dataset We use a larger population graph dataset from the UK Biobank (UKBB) (Sudlow et al., 2015) that consists of features extracted from brain magnetic resonance (MR) images. To extract the features, we follow the approach from Cole (2020), resulting in 68 imaging features and 20 non-imaging features for each subject. We use a set of 6406 subjects and perform a regression task for age prediction on this dataset. The mean age of this dataset is 62.86 years. We use this dataset to explore the difference in model performance when only using the imaging features compared to using all features. If not specifically specified, we only use the 68 imaging features.

UKBB Cardiac Dataset We extract another dataset from the UKBB (Sudlow et al., 2015) containing imaging features from cardiac MRIs as well as clinical features, on which we perform a binary classification of whether a subject suffers from cardiovascular diseases or not. We extract 6 non-imaging features and 86 imaging features using the pipeline from Bai et al. (2020) and create a population graph with 2900 subjects.

4.2 Graph Construction Methods

We use distinct graph construction methods for population graphs and compare their impact on the performance of different GNNs. We note that the here utilised methods are not extensive but we picked the most representative and most frequently used and well-established methods for static and dynamic graph construction.

4.2.1 Static Graph Construction

Using static graph construction methods refers to constructing a graph structure for the population graph that stays constant over the course of GNN training. There are several methods to construct a static population graph structure, while the most commonly used one utilises a k-nearest neighbour approach (Cunningham & Delany, 2021).

Self-loops Only To get an intuition about the impact of the graph structure on the GNN, we evaluate a GNN on a graph that is not really a graph but only contains self-loops. The adjacency matrix of a graph that only contains self-loops is equivalent to the identity matrix. In this setting, no message passing among nodes is performed since there are no connections between nodes. We use this setting to simulate a transductive learning setting without using a graph structure.

Random Graph Secondly, we construct a random graph structure by generating an Erdos-Rényi Graph with an edge probability of 0.001. We choose to evaluate all methods applied to a graph with a random graph structure in order to investigate the impact of the graph structure on model performance.

k-Nearest Neighbour Graph The most frequently used approach of graph construction for population graphs is the k-Nearest Neighbour (k-NN) approach. Here, k is a hyperparameter and defines the number of neighbours each node has. For this approach, different distance measures can be used, for example, the Euclidean distance or the cosine similarity. We use the implementation of *knn_graph* from Pytorch Geometric (Fey & Lenssen, 2019) and refer to the usage of the Euclidean distance as "k-NN Eucl." and the usage of the cosine similarity as "k-NN Cosine" in the tables below.

4.2.2 Dynamic Graph Construction

Dynamic graph construction refers to the learning of the graph structure in an end-to-end manner in parallel to the model training. There exist a few dynamic graph construction methods; however, for population graphs, mostly the approach from Kazi et al. (2022) is used. We here use the dDGM method, which uses a differentiable graph construction method that allows for an end-to-end learning of the graph structure during GNN training. In their work, Kazi et al. (2022) propose two differentiable graph learning modules: cDGM and dDGM. We here only use the dDGM implementation, since both in their work and in our preliminary results and related works like (Mueller et al., 2023a), dDGM resulted in better performance. The dDGM module can be applied to arbitrary initial graph structures. We evaluate the impact of the initial graph structure on the model performance by using different graphs as a starting point. For the CORA dataset, we evaluate dDGM starting off with **(a)** no edges, **(b)** only self-loops, **(c)** a random graph structure, **(d)** a k-NN graph, and **(e)** the original edges of the dataset, if available.

4.3 Graph Assessment

In order to gain insights into the constructed graph structures and investigate their "quality", we evaluate two graph assessment metrics: node homophily (Pei et al., 2020) and cross-class neighbourhood similarity (CCNS) (Ma et al., 2021). We follow the approach from Mueller et al. (2023a) and evaluate the *CCNS distance*, the there-defined homophily for regression tasks, and split the evaluation of all metrics into train and test nodes. The latter can be useful to investigate how differently the graph structure impacts training and test nodes.

4.4 Model Architectures and Training

We use two different model architectures in our experiments. For all dynamic graph construction experiments we use the architecture proposed by Kazi et al. (2022), which consists of two graph convolutional networks: a graph embedding function f and a diffusion function g. Following the results from the original paper (Kazi et al., 2022), we use the respective graph convolutions for both modules. For the static graph construction experiments, we use a GNN with 1, 2, or 3 graph convolutional layers (e.g. GCN or GraphSAGE), followed by an MLP. We use two sets of hyperparameters regarding the layers of these networks that can be found in the Appendix. During preliminary experiments, we noticed that using the same architecture for static graph

construction results in strong over-fitting of the models to the training sets. We, therefore, use a different architecture for the static graph construction experiments than for the dynamic ones. More details about all architectures can be found in the appendix. In all architectures, we utilise four different frequently used graph convolutions, namely graph convolutional networks (GCNs) (Kipf & Welling, 2016), graph SAGE networks (Hamilton et al., 2017), higher-order GNNs (GraphConv) (Morris et al., 2019), and graph attention networks (GATs) (Veličković et al., 2017). They all differ in the methodology of how the message-passing scheme is performed and their formal definitions can be found in Section 2.3. For the neural sheaf diffusion models, we utilise the setup of the original work, varying between the following sheaf models: *BundleSheaf*, *DiagSheaf*, and *GeneralSheaf*.

All models are trained in a transductive setting, where all nodes are available during training. We define a fixed set of hyperparameters for all experiments and run a hyperparameter search for at least 200 runs using sweeps from *Weights and Biases* (Biewald, 2020). We then pick the run with the best validation accuracy/MAE and evaluate its performance over 5 random seeds and report the mean test accuracy with the standard deviation. All trainings are performed on an Nvidia Quadro RTX 8000 GPU, using `Pytorch lightning` and `Pytorch Geometric` (Fey & Lenssen, 2019). All hyperparameters can be found in the appendix.

5 Experiments and Results

In this section, we summarise the experiments on all eight datasets with different graph construction methods, including static and dynamic graph construction and Neural Sheaf Diffusion models. We (1) summarise the overall best-performing GNNs for all datasets and compare them to three different baselines, (2) compare our results to different state-of-the-art (SOTA) population graph studies, (3) report the results of extensive studies on different SOTA graph learning methods for population graph datasets, (4) evaluate the method of GNNs for multi-modal data integration, and (5) evaluate the impact of the graph structure on the performance of GNNs for population graphs. The most noteworthy finding of our work is possibly the fact that simple baseline methods outperform more complex graph learning techniques on all tested population graph datasets.

5.1 Baselines Achieving Comparable Performance to GNNs

During an extensive evaluation of the performance of GNNs on medical population graphs, we found that most of the baselines reported in previous works are reported to have lower performance compared to the same or the best-performing baselines in our experiments. In fact, when optimally tuning three baseline models (random forest, linear/logistic regression, and ridge classifier/regression), we found that they perform competitively on all datasets (see Table 2). We compare their results to the performance of the best GNN as well as a Neural Sheaf Diffusion model –either trained by ourselves or reporting the results from the respective works (indicated by the reference in Table 2). All results are summarised in Table 2, where the best model for each dataset is highlighted in bold. For the benchmark citation network datasets (CORA, CITESEER, PUBMED), we use only the node features of the original graph for the evaluation of the baseline models.

It is noteworthy that for all population graph datasets apart from the UKBB Brain Age dataset, at least one of the baseline methods outperforms the best GNN model. On the UKBB brain age dataset, the GNN slightly outperforms the ridge regression (best baseline) by an MAE of 0.066. However, a two-sided t-test between the results of the best GNN and the strongest baseline (ridge regression) did not show a significant difference in performance with a p-value of 0.06. These results raise the main question of this work: *"Are population graphs really as powerful as believed?"* Our results indicate the contrary and we investigate the discrepancy between our work and related works in the following sections, discussing potential reasons for this gap between (a) reported baselines in different works and ours and (b) baseline algorithms and GNNs on population graphs in general.

5.2 Comparison to Other Published Results

In order to validate the results of these findings, we compare our results to published results in the most closely related works, investigating the different performances of baseline models and GNNs on different datasets. We compare the benchmark citation networks and TADPOLE, ABIDE, and UKBB brain age datasets.

Table 2: **Summary of results** of different baseline methods and the best GNNs and Neural Sheaf Models, either from our training evaluated on 5 random seeds or from literature ([1]: Kazi et al. (2022), [1]: Parisot et al. (2017), [3]: Bodnar et al. (2022)). CORA, CITESEER, and PUBMED are benchmark citation networks, the remaining datasets are medical population graphs. For the citation network datasets, we evaluate GNNs on graphs with original edges (orig. edges) and on graphs constructed using k-NN (GNN k-NN). All reported values are the accuracy on the test set, apart from the regression dataset UKBB Brain Age, here we report the MAE.

Method	CORA	CITESEER	PUBMED	TADPOLE	Brain Age	Cardiac	COVID	ABIDE
Random forest	0.7788 ± 0.00	0.7480 ± 0.01	0.7286 ± 0.01	**0.9474 ± 0.00**	3.7913 ± 0.01	**0.7061 ± 0.01**	0.8250 ± 0.02	**0.7046 ± 0.01**
Ridge	0.7860 ± 0.00	**0.7720 ± 0.00**	0.7350 ± 0.00	0.7368 ± 0.00	3.4185 ± 0.00	0.6935 ± 0.00	**0.8750 ± 0.00**	0.7014 ± 0.00
Linear/Logistic	0.5750 ± 0.00	0.5600 ± 0.00	0.7310 ± 0.00	0.8421 ± 0.00	3.4287 ± 0.00	0.6858 ± 0.00	0.8125 ± 0.00	0.6290 ± 0.00
GNN k-NN	0.7692 ± 0.01	0.6908 ± 0.01	0.6908 ± 0.01	0.9404 ± 0.02	**3.3524 ± 0.06**	0.6970 ± 0.02	0.7875 ± 0.03	0.695 [2]
GNN orig. edges	0.8540 ± 0.01	0.7548 ± 0.01	0.8760 ± 0.01 [1]	-	-	-	-	-
Neural Sheaf	**0.8730 ± 0.01** [3]	0.7714 ± 0.02 [3]	**0.8949 ± 0.00** [3]	0.9368 ± 0.02	-	0.6904 ± 0.01	0.8000 ± 0.03	0.5448 ± 0.01

The related works we pick for comparison are works introducing the concept of population graphs Parisot et al. (2017), as well as new graph learning techniques, that have been applied to or designed for population graph studies Kazi et al. (2019; 2022); Bintsi et al. (2023a). The results are summarised in Table 3. All our baselines outperform the published baselines in the related works, while our GNN implementations match the performances reported in the respective works. This corroborates our hypothesis that our implementation is on par with previously reported works, while these works seem to underestimate the baseline performance.

The discrepancy in baseline performance can partially be due to different models, different hyperparameters, or the utilisation of only a subset of the features for the evaluation of the baselines. Some works, for example, only use the node features of the GNN as input for the baseline, while using additional features for the edge construction of the population graph. We deem this to be an unfair comparison and always use all features that we use for graph construction and as node features as input for the baseline. For the evaluation of the baseline methods on the benchmark citation network datasets, we use only the node features of the graphs since the edges cannot be incorporated in the same feature vector in a straightforward way. Some works do not specify on which features the baseline is evaluated Parisot et al. (2017).

Table 3: Comparison of our results to results from related works Parisot et al. (2017) ([1]), Kazi et al. (2022) ([2]), Kazi et al. (2019) ([3]), and Bintsi et al. (2023a) ([4]). The overall best result for each dataset is underlined. The baseline for the UKBB Brain Age dataset is a ridge regression for our work and a linear regression for the results from Bintsi et al. (2023a); for the TADPOLE dataset: Linear classifier for results from Kazi et al. (2022), random forest for our results; for ABIDE: Ridge regression for results from Parisot et al. (2017), random forest for our results. All our baselines outperform reported baselines in other works, while our GNN implementations match performance.

Dataset	Score	Method	Convolution	Other reported results	Our results
CORA	Accuracy ↑	dDGM [2]	GCN	0.8240 ± 0.01 [2]	**0.8372 ± 0.01**
			GAT	0.8130 ± 0.03 [2]	**0.8388 ± 0.04**
CITESEER	Accuracy ↑	dDGM [2]	GCN	0.7480 ± 0.01 [2]	**0.7548 ± 0.01**
			GAT	**0.7400 ± 0.01** [2]	0.7396 ± 0.01
TADPOLE	Accuracy ↑	Baseline	-	0.7022 ± 0.06 [2]	**0.9474 ± 0.00**
		dDGM [2]	GCN	**0.9414 ± 0.02** [2]	0.9333 ± 0.01
		InceptionGCN [3]	InceptionGCN	0.8435 ± 0.07 [3]	-
UKBB Brain Age	MAE ↓	Baseline	-	3.82 [4]	**3.5063 ± 0.00**
		dDGM [2]	GCN	**3.72** [4]	3.8287 ± 0.03
		dDGM [2]	SAGE	-	**3.5034 ± 0.06**
		adaptive [4]	GCN	3.62 [4]	-
ABIDE	Accuracy ↑	Baseline	-	0.668 [1]	**0.7040 ± 0.01**
		Similarity Score [1]	GCN	0.695 [1]	-
		InceptionGCN [3]	InceptionGCN	0.6923 ± 0.07 [3]	-

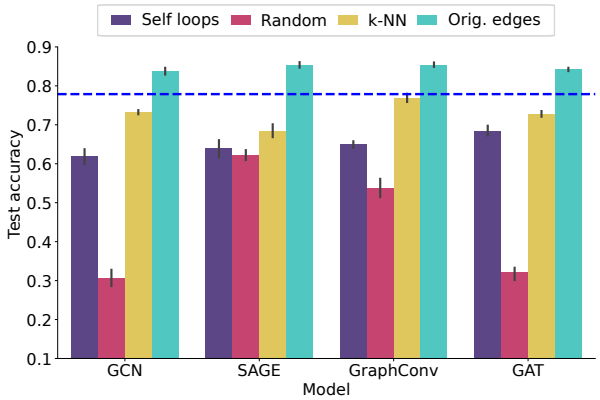
5.3 Benchmark Citation Network Datasets

We first evaluate commonly used graph construction methods for population graph studies on frequently used benchmark citation datasets CORA, CITESEER, and PUBMED (Yang et al., 2016). They provide a "ground truth" graph structure, which we can evaluate in comparison to the graphs resulting from graph construction methods used for population graph studies. This allows us to investigate how the different graph construction methods perform compared to a given "ground-truth" adjacency matrix. The results of the best-performing GNNs and baselines on all three datasets are summarised in Table 2. We exemplarily summarise the results of more extensive studies on the CORA dataset in Table 4. We here only use three graph construction methods: random, k-NN with Euclidean distance, and the original edges. Further experiments can be found in the Appendix. We compare the graph learning-based methods to simple baselines (blue): a random forest, a ridge classifier, and a multi-layer perceptron (MLP). The ridge classifier achieves a test accuracy of 78.60%. All methods that outperform the best baseline are underlined and the overall best performance for static and dynamic graph construction methods are highlighted in bold. The performance of the different graph convolutional models and under static and dynamic graph construction are furthermore visualised in Figures 3a and 3b. We can see that using the original graph structure leads to the best model results, both under static and dynamic graph construction. The method of generating a k-NN graph, which is most frequently used for population graphs performs on pair with the baseline and often even under-performs the baseline. Using a random graph structure or a k-NN graph negatively impacts model performance, both in the static and dynamic cases. We attribute this to the fact that the homophily of the constructed k-NN graphs is close to 0.5, which is a highly challenging graph structure for graph learning (Zhu et al., 2020). Also, the CCNS distance of these graphs is comparably high and improves further when applying dynamic graph construction methods, where the graph structure can be adapted to the learning task. However, in some cases, the dynamic graph construction method leads to a large difference between the homophily and CCNS distance of the training nodes and the test nodes. This can, for example, be seen in the case of an initialised graph without edges and the GCN model. Here, the train homophily of the resulting learned graph is very high at 0.987, while the test homophily stays comparably low at 0.749. This is one of the potential pitfalls of dynamic graph construction methods, that the model only optimises the graph structure for the training nodes, disregarding the graph structure of the test nodes. We furthermore observe that GCN and GAT networks are highly sensitive to the graph structure, while GraphSAGE and GraphConv still achieve comparable results, even on a random graph structure.

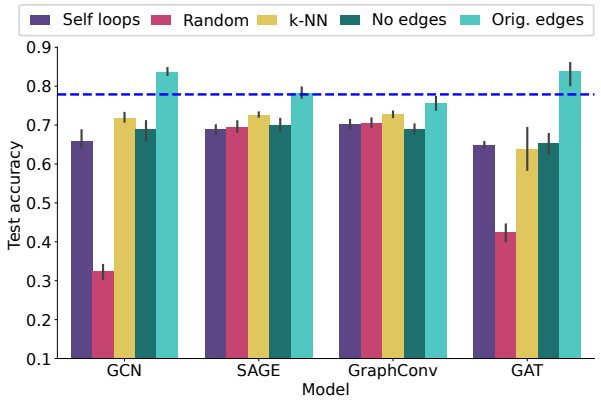
The overall best score on the CORA dataset is achieved with the static graph construction and the original edges of the dataset, using SAGE and GraphConv. When using neural sheaf diffusion models instead of commonly used GNNs, these results can even be improved. The authors of Bodnar et al. (2022) report an accuracy of 0.8730 ± 0.01 on the CORA dataset. The experiments on all benchmark citation network datasets have shown that GNNs can improve performance compared to simple baseline methods. However, even for the CITESEER dataset (see Table 2), a ridge classifier outperforms all GNN methods and neural sheaf diffusion networks.

5.4 Medical Population Graphs

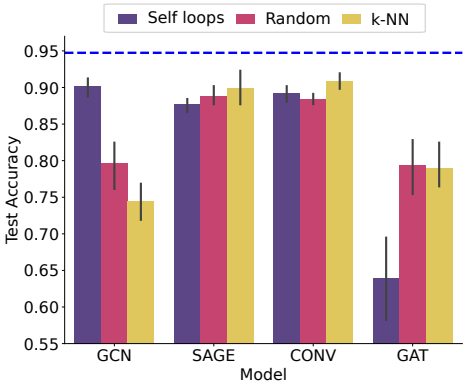
The results on the TADPOLE dataset are summarised in Table 5 and visualised in Figures 3c and 3d. None of the GNNs outperform the best baseline method, which in this case is a random forest. This is even the case in settings where the homophily of the test set is very high like, for example, for the static k-NN graph construction and the GAT convolution. However, we recall that the methods we use here match performance to related works such as Kazi et al. (2019; 2022); Parisot et al. (2017). We observe similar results on the UKBB brain age dataset. We here perform age regression on the imaging features only and report the MAE as model performances. The results are summarised in Table 6 and visualised in Figures 3e and 3f. We do not report the CCNS values for this dataset, since CCNS is not defined for regression tasks. SAGE and GraphConv networks do not seem to be influenced by the randomness of the graph structure and are still able to learn meaningful representations of the node features and make accurate predictions. The homophily of the k-NN graphs generated for the UKBB dataset is also quite high, similar to the TADPOLE dataset. The same holds for its low CCNS distance score. We furthermore observe that GCN models tend to perform better at a lower number of neighbours. Interestingly, here the best-performing model is still the SAGE GNN,



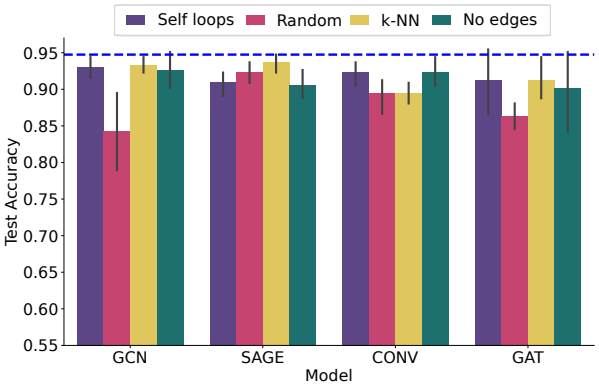
(a) **Static** graph construction on **CORA**



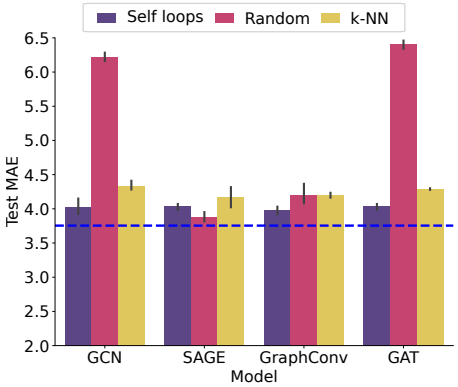
(b) **Dynamic** graph construction on **CORA**



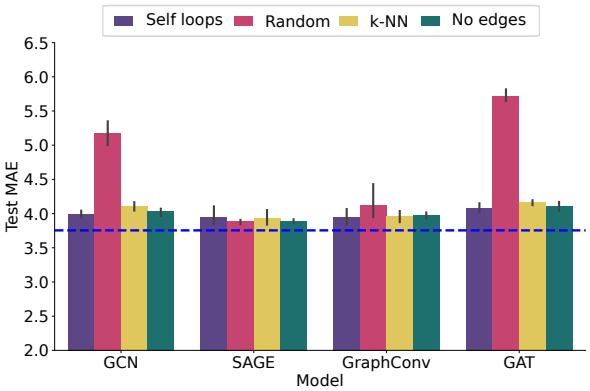
(c) **Static** graph construction on **TADPOLE**



(d) **Dynamic** graph construction on **TADPOLE**



(e) **Static** graph construction on **UKBB Brain Age**



(f) **Dynamic** graph construction on **UKBB Brain Age**

Figure 3: **Results of the experiments** on all datasets with static graph construction (left column) and dynamic graph construction (right column). First row: **CORA**, second row: **TADPOLE**, third row: **UKBB brain age**. For the classification dataset CORA and TADPOLE, we report the test accuracy (higher is better); For the regression task on the UKBB brain age, we report the test MAE (lower is better). The mean performance of the baseline is indicated by the dashed blue lines.

Table 4: Results of the experiments on the **CORA** dataset. BL: baselines, k: number of neighbours. GNNs out-performing the baseline are underlined, and the best performances of static and dynamic graph constructions, highest homophily, and lowest CCNS distance are **bold**.

	Initial edges	Model	k	Test acc	Homophily ↑ Train	Homophily ↑ Test	CCNS distance ↓ Train	CCNS distance ↓ Test
BL	-	Random Forest	-	0.7788 ± 0.00	-	-	-	-
		Ridge classifier	-	0.7860 ± 0.00	-	-	-	-
		MLP	-	0.6030 ± 0.00	-	-	-	-
Static graph construction	Random	GCN	-	0.3068 ± 0.02	0.171 ± 0.26	0.201 ± 0.29	0.373	0.356
		SAGE	-	0.6224 ± 0.02	0.171 ± 0.26	0.201 ± 0.29	0.373	0.356
		GraphConv	-	0.5388 ± 0.03	0.171 ± 0.26	0.201 ± 0.29	0.373	0.356
		GAT	-	0.3208 ± 0.02	0.171 ± 0.26	0.201 ± 0.29	0.373	0.356
	k-NN Euclidean	GCN	20	0.7336 ± 0.01	0.498 ± 0.23	0.495 ± 0.22	0.378	0.396
		SAGE	20	0.6836 ± 0.02	0.498 ± 0.23	0.495 ± 0.22	0.378	0.396
		GraphConv	20	0.7692 ± 0.01	0.498 ± 0.23	0.495 ± 0.22	0.378	0.396
		GAT	20	0.7288 ± 0.01	0.498 ± 0.23	0.495 ± 0.22	0.378	0.396
	Orig edges	GCN	-	0.8372 ± 0.01	**0.830 ± 0.29**	**0.860 ± 0.29**	**0.101**	**0.084**
		SAGE	-	**0.8540 ± 0.01**	**0.830 ± 0.29**	**0.860 ± 0.29**	**0.101**	**0.084**
		GraphConv	-	**0.8540 ± 0.01**	**0.830 ± 0.29**	**0.860 ± 0.29**	**0.101**	**0.084**
		GAT	-	0.8420 ± 0.00	**0.830 ± 0.29**	**0.860 ± 0.29**	**0.101**	**0.084**
Dynamic graph construction	No edges	GCN	2	0.6900 ± 0.03	**0.987 ± 0.10**	0.749 ± 0.42	**0.072**	0.181
		SAGE	2	0.7000 ± 0.02	0.589 ± 0.38	0.510 ± 0.37	0.232	0.267
		GraphConv	2	0.6904 ± 0.01	0.880 ± 0.21	0.769 ± 0.25	0.085	0.144
		GAT	2	0.6532 ± 0.03	0.921 ± 0.20	0.652 ± 0.43	0.050	0.208
	Random	GCN	2	0.3240 ± 0.02	0.663 ± 0.28	0.230 ± 0.38	0.201	0.351
		SAGE	10	0.6960 ± 0.01	0.674 ± 0.25	0.534 ± 0.32	0.206	0.323
		GraphConv	2	0.7052 ± 0.01	0.831 ± 0.24	0.719 ± 0.25	0.101	0.180
		GAT	10	0.4252 ± 0.02	0.405 ± 0.23	0.252 ± 0.23	0.436	0.544
	k-NN Euclidean	GCN	5	0.7192 ± 0.01	0.581 ± 0.31	0.533 ± 0.30	0.314	0.363
		SAGE	5	0.7264 ± 0.01	0.838 ± 0.23	0.676 ± 0.35	0.097	0.222
		GraphConv	5	0.7284 ± 0.01	0.884 ± 0.21	0.801 ± 0.24	0.073	**0.129**
		GAT	20	0.6388 ± 0.06	0.419 ± 0.27	0.415 ± 0.28	0.429	0.446
	Orig edges	GCN	20	**0.8372 ± 0.01**	0.861 ± 0.24	**0.813 ± 0.31**	0.086	0.133
		SAGE	10	0.7832 ± 0.01	0.958 ± 0.10	0.780 ± 0.32	0.019	0.138
		GraphConv	2	0.7576 ± 0.02	0.819 ± 0.25	0.780 ± 0.29	0.115	0.149
		GAT	2	0.8388 ± 0.04	0.885 ± 0.21	0.807 ± 0.29	0.071	0.131

which is trained on a random graph structure and under static graph construction, followed by the SAGE model with random graph initialisation and dynamic graph construction. We also cannot see a clear benefit of using dynamic graph construction methods on all datasets. While the best dynamic result outperforms the best static result on the TADPOLE dataset, static methods achieve higher results on the UKBB brain age dataset.

In these experiments, we can see again that SAGE and GraphConv are less impacted by the graph structure and that the dynamic graph construction helps in improving the graph structure from an initial random graph (with low homophily) to one with higher homophily. The latter happens especially for GCN and GAT models, which are highly sensitive to the graph structure and therefore benefit most from a graph structure with higher homophily.

5.5 Population Graphs for Multi-Modal Data Integration

One highly emphasised advantage of population graphs is their utilisation for multi-modal data integration (Parisot et al., 2017; Zheng et al., 2022; Keicher et al., 2021). In one of the first utilisations of population graphs (Parisot et al., 2017), for instance, a graph construction method is introduced that uses clinical features to generate the edges between subjects, while image-derived features are used as node features in the graph. In later approaches, especially for dynamic graph construction, methods moved away from a clear separation between clinical and image-derived features (Kazi et al., 2022). We scrutinise this claimed advantage of population graphs and argue that all available features can easily be appended and therefore incorporated into the node features. The only exception to this is when images are used directly as node features –not only extracted image features. However, this setup comes with large memory requirements and has not been studied in detail.

Table 5: Results of the experiments on the **TADPOLE** dataset. GC: graph construction, BL: baselines, k: number of neighbours. The best performance for each method is bold.

	Initial edges	Model	k	Test acc ↑	Test homophily ↑	Test CCNS distance ↓
BL	-	Majority vote	-	0.5674 ± 0.00	-	-
	-	Random forest	-	**0.9474 ± 0.00**	-	-
	-	Logistic regression	-	0.8597 ± 0.00	-	-
Static GC	Random	GCN	-	0.7965 ± 0.04	0.426 ± 0.49	0.348
		SAGE	-	0.8877 ± 0.01	0.426 ± 0.49	0.348
		GraphConv	-	0.8842 ± 0.01	0.426 ± 0.49	0.348
		GAT	-	0.7930 ± 0.04	0.426 ± 0.49	0.348
	k-NN Euclidean	GCN	5	0.7439 ± 0.03	0.775 ± 0.24	0.213
		SAGE	5	0.8982 ± 0.03	0.775 ± 0.24	0.213
		GraphConv	5	**0.9088 ± 0.01**	0.775 ± 0.24	0.213
		GAT	2	0.7895 ± 0.04	**0.904 ± 0.20**	**0.094**
Dynamic GC	No edges	GCN	20	0.9263 ± 0.03	**0.919 ± 0.19**	0.073
		SAGE	20	0.9053 ± 0.02	0.806 ± 0.21	0.183
		GraphConv	2	0.9228 ± 0.02	0.798 ± 0.34	0.190
		GAT	20	0.9018 ± 0.06	0.908 ± 0.15	**0.101**
	Random	GCN	2	0.8421 ± 0.06	0.851 ± 0.27	0.177
		SAGE	10	0.9228 ± 0.02	0.423 ± 0.22	0.616
		GraphConv	5	0.8947 ± 0.03	0.411 ± 0.25	0.594
		GAT	5	0.8632 ± 0.02	0.895 ± 0.20	0.119
	k-NN Euclidean	GCN	2	0.9333 ± 0.01	0.793 ± 0.28	0.204
		SAGE	20	**0.9368 ± 0.01**	0.461 ± 0.63	0.632
		GraphConv	10	0.8947 ± 0.02	0.777 ± 0.29	0.219
		GAT	10	0.9123 ± 0.03	0.775 ± 0.29	0.206

Table 6: Results of the experiments on the **UKBB Brain Age** imaging dataset. BL: baselines, k: number of neighbours, GC: graph construction. The best performance for static and dynamic graph construction and the respective highes homophily is **bold**.

	Initial edges	Model	k	Test MAE ↓	Test homophily ↑
BL	-	Mean prediction	-	6.4090 ± 0.00	-
	-	Random Forest	-	4.1424 ± 0.01	-
	-	Linear Regression	-	3.7545 ± 0.00	-
Static GC	Random	GCN	-	6.2158 ± 0.07	0.742 ± 0.10
		SAGE	-	**3.8764 ± 0.08**	0.742 ± 0.10
		GraphConv	-	4.2029 ± 0.16	0.742 ± 0.10
		GAT	-	6.4034 ± 0.07	0.742 ± 0.10
	k-NN Euclidean	GCN	2	4.3351 ± 0.07	**0.916 ± 0.07**
		SAGE	10	4.1780 ± 0.17	0.844 ± 0.06
		GraphConv	2	4.1979 ± 0.04	**0.916 ± 0.07**
		GAT	20	4.2888 ± 0.01	0.834 ± 0.06
Dynamic GC	No edges	GCN	2	4.0257 ± 0.06	**0.865 ± 0.10**
		SAGE	5	3.8882 ± 0.03	0.754 ± 0.10
		GraphConv	5	3.9741 ± 0.05	0.840 ± 0.08
		GAT	2	4.1071 ± 0.07	0.843 ± 0.11
	Random	GCN	2	5.1712 ± 0.20	0.834 ± 0.13
		SAGE	10	**3.8811 ± 0.04**	0.780 ± 0.09
		GraphConv	10	4.1248 ± 0.30	0.768 ± 0.09
		GAT	2	5.7138 ± 0.10	0.831 ± 0.14
	k-NN Euclidean	GCN	2	4.1109 ± 0.07	0.849 ± 0.11
		SAGE	20	3.9226 ± 0.13	0.842 ± 0.07
		GraphConv	2	3.9560 ± 0.09	0.831 ± 0.11
		GAT	2	4.1603 ± 0.04	0.837 ± 0.11

We perform several experiments investigating whether GNNs are useful for multi-modal data integration for population graphs. We take the two UKBB datasets and evaluate the performance of GNNs with different combinations of imaging and non-imaging features for graph construction and as node features. The results are summarised in Table 7. Given that the graph convolutions SAGE and GraphConv performed best in our previous experiments on population graphs, we limit these results to those two convolutions. The

best performing GNN is highlighted in bold, the second best in purple, and the third best in green. The corresponding homophily values for each graph structure for both datasets are summarised in Table 8. For these experiments with static graph construction, we experiment with a different model architecture consisting of only one graph convolutional layer, followed by an MLP.

We can see that for the brain age dataset, the best GNN is the one that uses all available features as node features and for edge construction. The second and third-best GNNs also use all features as node features. For the cardiac dataset, the best and second-best models also use all features as node features, however, the third-best model uses only the imaging features as node features and the non-imaging features for edge construction. Furthermore, on the UKBB brain age dataset, some GNNs outperform the respective baseline (which only uses the node features) by small margins. This is not the case for the cardiac dataset. Here none of the GNNs outperform the respective baselines. Interestingly, on the UKBB brain age dataset, the static graph construction results in better performance than dynamic graph construction, which is the opposite for the cardiac dataset. We can also see that the node features slightly dominate the prediction, such that the performance of the GNN somewhat matches the performance of the baseline that uses the node features only. This is reasonable since the specific features that are used for edge construction are reduced into a simple "measure of similarity". However, overall the baselines perform on par with the GNNs.

Table 7: Results of different combinations of image-derived and non-imaging features as node features and for graph construction on the UKBB brain age and cardiac datasets. For the age prediction dataset, the baseline is a ridge regression, for the cardiac dataset a random forest. GNN outperforms their corresponding node-feature-baseline are underlined. Best GNN: **bold**, second best GNN: purple, third best GNN: green.

	Features		Model	UKBB Brain Age Test MAE ↓		UKBB Cardiac Test accuracy ↑	
Baseline	-		Naive baseline	6.4090		0.5000	
	Non-imaging		Best baseline	4.6509 ± 0.00		0.6678 ± 0.00	
	Imaging			3.5063 ± 0.00		0.6969 ± 0.01	
	All			3.4185 ± 0.00		**0.7046 ± 0.01**	
	Node Features	**(Initial) Edges**	**Model**	**dDGM test MAE ↓**	**Static test MAE ↓**	**dDGM test acc. ↑**	**Static test acc. ↑**
Graph Neural Networks	All	All	SAGE	3.5034 ± 0.06	3.4351 ± 0.00	0.6816 ± 0.01	0.6609 ± 0.02
			GraphConv	3.5407 ± 0.04	**3.3524 ± 0.06**	0.6785 ± 0.01	0.6705 ± 0.01
	All	Imaging	SAGE	3.5471 ± 0.02	3.4249 ± 0.00	**0.6839 ± 0.01**	0.6739 ± 0.01
			GraphConv	3.5221 ± 0.03	3.3758 ± 0.05	0.6690 ± 0.01	0.6743 ± 0.01
	All	Non-imaging	SAGE	3.5317 ± 0.04	3.4175 ± 0.00	0.6724 ± 0.01	0.6632 ± 0.01
			GraphConv	3.6792 ± 0.25	3.4330 ± 0.01	0.6751 ± 0.01	0.6644 ± 0.02
	Imaging	Imaging	SAGE	3.9226 ± 0.13	3.7716 ± 0.04	0.6743 ± 0.01	0.6705 ± 0.00
			GraphConv	3.9560 ± 0.09	3.8368 ± 0.00	0.6632 ± 0.01	0.6628 ± 0.01
	Imaging	Non-imaging	SAGE	3.9130 ± 0.05	3.6791 ± 0.01	0.6567 ± 0.01	0.6785 ± 0.00
			GraphConv	3.9835 ± 0.01	3.7099 ± 0.04	0.6805 ± 0.01	0.6483 ± 0.01
	Non-imaging	Imaging	SAGE	4.6767 ± 0.06	4.9382 ± 0.00	0.6755 ± 0.01	0.6521 ± 0.01
			GraphConv	4.0376 ± 0.12	5.0410 ± 0.02	0.6579 ± 0.01	0.6452 ± 0.01

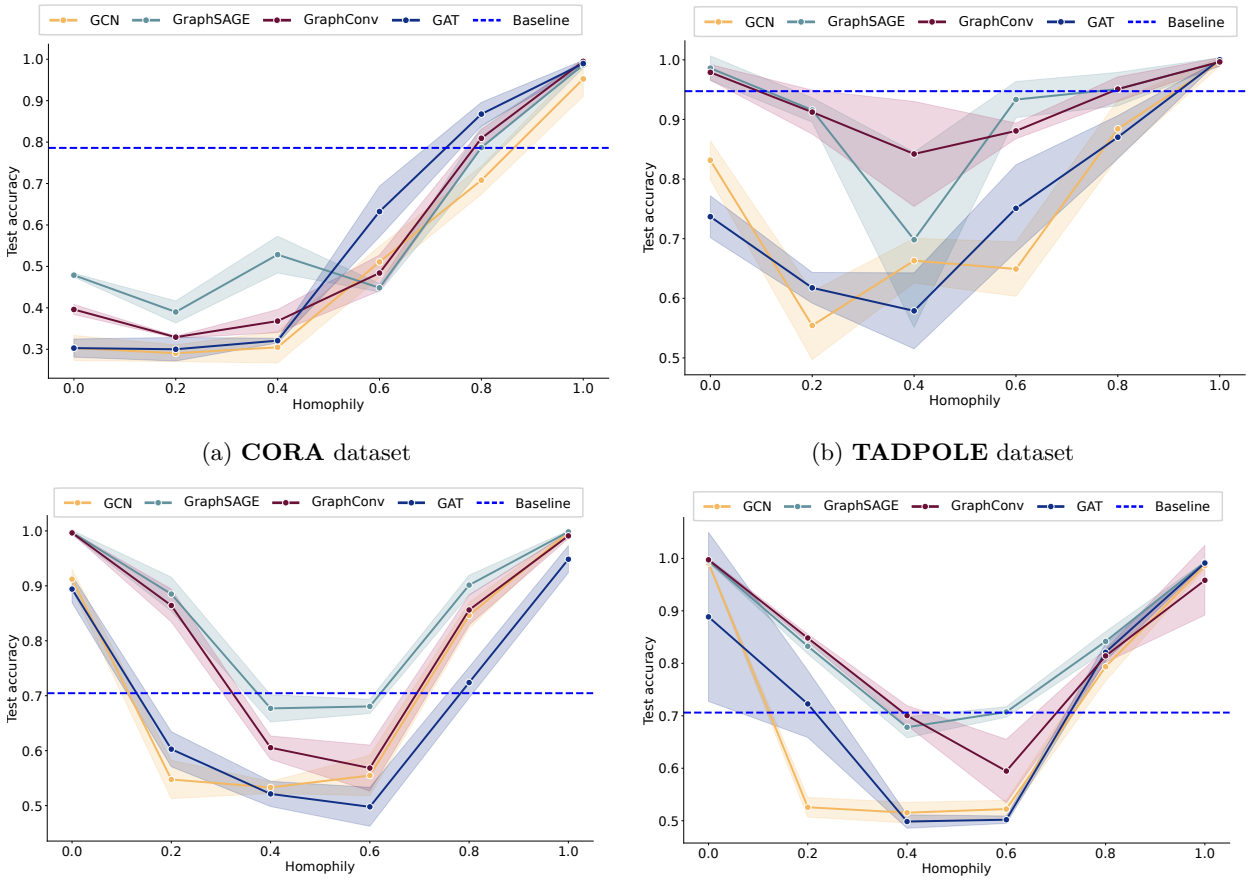
5.6 Impact of the Graph Structure on Model Performance

Several works have shown that the "quality" of the graph structure has a significant impact on the performance of graph neural networks (Luan et al., 2022; Zhu et al., 2020). We investigate this in the context of population graphs with two specific graph assessment metrics: node homophily and cross-class neighbourhood similarity. The graph metrics for the experiments in the former sections are in the Tables 4, 5, and 6. The homophily values of the graph structures constructed from different combinations of image and non-image features for the UKBB brain age and cardiac dataset are summarised in Table 8. We can see that for both datasets, all graph structures have similar homophily values, which might be the reason why the performance of all graph structures is very similar when using all node features.

Different Types of Graph Convolution Zhu et al. (2020) have shown interesting correlations between homophily and different graph convolutions. They showed that the separate handling of node features of the node of interest (x_i) and its neighbouring nodes ($\mathcal{N}_i$) improves the performance of GNNs on heterophilic graphs. The same accounts for networks that evaluate the k-hop neighbourhoods separately. Graph convolutional networks (GCNs) (Kipf & Welling, 2016) do not separate node features of i and $\mathcal{N}_i$, but average the message

Table 8: Homophily values of the **UKBB brain age** and **cardiac** datasets with $k = 5$ and the k-NN graph construction, when using all features, only imaging, or only non-imaging features for graph construction.

Dataset	Features	Homophily
Brain Age	All	0.8571 ± 0.07
	Imaging	**0.8619 ± 0.07**
	Non-imaging	0.8237 ± 0.08
Cardiac	All	0.6404 ± 0.22
	Imaging	0.6396 ± 0.22
	Non-imaging	**0.6649 ± 0.23**



(a) **CORA** dataset

(b) **TADPOLE** dataset

(c) **ABIDE** dataset

(d) **UKBB Cardiac** dataset

Figure 4: Performance of different graph convolutions on synthetic graph structures with different homophily values on (a) the **CORA** dataset, (b) the **TADPOLE** dataset, (c) the ABIDE dataset, and (d) the UKBB Cardiac dataset. The dashed blue line indicates the mean performance of the best baseline for each dataset.

passing over both in one step (see Equation 5). SAGE and GraphConv on the other hand distinguish between x_i and $x_j, j \in \mathcal{N}_i$ (Equations 6 and 7). GAT (Equation 8) learns different attention coefficients for x_i and $x_j, j \in \mathcal{N}_i$. However, the weights of the network are shared for both, which might negatively impact performance on graphs with low homophily.

Our experiments support these findings. We see that GCN and GAT seem to be strongly affected by the graph structure whereas SAGE or GraphConv networks perform more consistently across different graph structures.

Different Datasets The impact of the homophily on the model performance is not only dependent on the graph convolution but also varies depending on the dataset, probably related to the number of classes in the dataset as well as class imbalance. In order to investigate this, we perform experiments with synthetic graph structures on the TADPOLE dataset (3 classes), the CORA dataset (7 classes), the UKBB cardiac dataset (2 classes), and the ABIDE dataset (2 classes) at different synthetically generated homophily values. Figure 4 shows the performance of different graph convolutions on 3-layer GNNs using static graph construction on the different datasets. For the CORA dataset (Figure 4a), all models perform worse than the baseline with homophily values lower than 0.8. While all graph convolutions are impacted similarly and perform worse than the baseline for low-homophily graphs, SAGE and GraphConv reach better performance than GAT and GCN. The low-homophily graphs do not allow the model to learn meaningful node feature embeddings, since during the course of training, node features of differently labelled nodes are averaged and shared, interfering with the model's goal to distinguish different classes. Interestingly, the performance for the TADPOLE dataset (Figure 4b) looks different. We observe see similar differences between the graph convolutions. However, we also observe that only at very high and very low homophily values, the GNN can outperform the baseline. Everything in between either matches the performance of the baseline or reaches a worse performance. When we now compare the homophily values of the generated graph structures in our experiments on the TADPOLE dataset above, we can see that most of them have a homophily of around 0.7 or 0.8. The other two datasets –ABIDE and UKBB cardiac– require a graph structure with lower homophily to outperform the baseline, however, the same pattern holds that all population graphs constructed in our experiments reached at homophily values in the range where the GNNs under-perform or perform on par with the baselines. This potentially explains why the population graphs do not outperform the graph-agnostic baseline models.

Furthermore, the high performance of the GNNs at low homophily values for the population graphs is highly different from that on the CORA dataset. We attribute this to the capability of the GNNs to learn the opposite labels from the majority of the neighbour labels, which we deem impossible for datasets with more classes. We investigate this further in the next section.

Attention Evaluation We attribute the relatively good performance of all models at low homophily values on the TADPOLE dataset (Figure 4b) to the learning of opposite labels for specific node features. If most of the neighbouring nodes share a different label than the one the node of interest holds, but this is consistent across the graph –the graph has a low CCNS distance–, then the network can still learn to make the correct predictions. We show this by evaluating the attention values of GAT networks of four synthetic graph structures with different homophily values, shown in Table 9. We always report the normalised sum of all attention heads of the GAT. At homophily 0.9 (where most neighbours share the same label as the node of interest), the attention from the neighbours with the same label is the highest. On the other hand, at hom = 0.5, all nodes receive the highest attention from neighbours with class label "MCI". This makes it very difficult for the network to distinguish between nodes of different labels, and therefore to make the correct predictions. At very low homophily (hom = 0.1), the attention of the neighbours with the same label is 0, which again, makes it possible for the network to distinguish nodes by their neighbourhood, enabling correct predictions. Three examples of 2-hop neighbourhoods at the different homophily values are visualised in Figure 5. The label is indicated by the node colour and the distance between two nodes indicates the attention value of this edge. While at hom = 0.9, most neighbours share the same label, at a low homophily value of 0.1 (c), most neighbours have a different label and the attention values are similar across them. At an in-between homophily of 0.4, several nodes share the same label, for others do not.

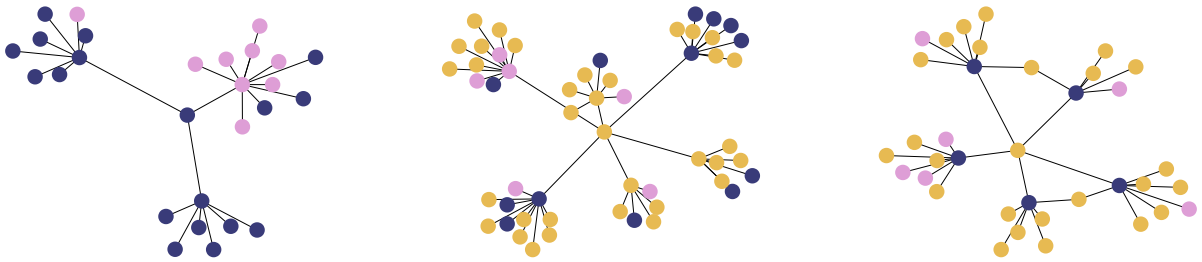
6 Discussion

In this work, we evaluate the performance of medical population graphs on three benchmark datasets and five population graph datasets and compare state-of-the-art graph learning techniques to well-tuned baseline models. We consistently observe the following three findings:

1. **GCN and GAT are poorly suited for population graph studies.** GNNs using GraphSAGE and GraphConv convolutions consistently outperform GCN and GAT models, which leads to the conclusion that the latter methods are not suitable for GNNs in population graph studies. We

Table 9: Mean and standard deviation of normalised attention values from all neighbours with respective labels of a graph structure with high and low homophily. The highest attention values for each node label class are highlighted in bold. NC: normal control, MCI: mild cognitive impairment, AD: Alzheimer's disease.

Homophily	Node label	Attention from NC	Attention from MCI	Attention from AD
0.9	NC	**1.919 ± 1.08**	0.532 ± 0.56	0.091 ± 0.21
	MCI	0.198 ± 0.31	**1.881 ± 1.06**	0.083 ± 0.22
	AD	0.158 ± 0.29	0.777 ± 0.66	**1.961 ± 1.14**
0.4	NC	0.978 ± 0.75	**2.002 ± 1.05**	0.255 ± 0.34
	MCI	0.556 ± 0.59	**0.972 ± 0.74**	0.243 ± 0.36
	AD	0.676 ± 0.68	**1.743 ± 0.97**	0.940 ± 0.71
0.1	NC	0.000 ± 0.00	**3.106 ± 1.47**	0.415 ± 0.48
	MCI	**0.985 ± 0.74**	0.000 ± 0.00	0.461 ± 0.57
	AD	1.038 ± 0.88	**3.013 ± 1.35**	0.000 ± 0.00



(a) Homophily 0.9 (b) Homophily 0.4 (c) Homophily 0.1

Figure 5: Visualisation of a random node (centre node) from the TADPOLE dataset with synthetically generated graph structures and its two-hop neighbourhood. The node colours indicate node labels and the distance is proportional to the summed attention weight of the edges to the respective neighbouring node.

attribute this to the fact that GCN and GAT networks are highly affected by the graph structure, whereas GraphSAGE and GraphConv networks are more robust in this regard. This also manifests in the fact that GCN and GAT networks benefit more from dynamic graph construction than the other two convolutions and that GraphSAGE and GraphConv models can perform equally well on random graph structures.

2. **The utilisation of population graphs with the goal of multi-modal data integration might not be as promising as believed.** We show that using all available features for edge construction and as node features might lead to better results and argue that a concatenation of all features is easily doable –except when using images as node features.

3. **None of the state-of-the-art GNN methods significantly outperform well-tuned baseline methods** (see Table 2). This raises the question of whether population graphs have any benefit over graph-agnostic models. In Section 5.6 we investigate the interplay of the graph structure and the performance of the GNNs on a population graph dataset and conclude that only a nearly perfect graph structure leads to a better performance of GNNs compared to baseline models, which has not been possible with the current graph construction methods in this research area.

Given that even a random graph structure can lead to comparable GNN performance to using a "meaningful" graph structure that is constructed using the k-NN approach, we conclude that creating a population graph with k-NN does not result in a "good-enough" graph structure. Especially for networks like SAGE and GraphConv, where the graph structure has comparably little impact on the model performance, the choice of the graph construction method does not show a strong influence on the results. We furthermore note that all baseline models are easy to implement using standard libraries such as `scikit-learn` (Pedregosa et al., 2011), are significantly faster to fit than the training of GNNs, and do not require extensive hyperparameter tuning.

7 Conclusion and Future Work

Medical population graphs were first introduced in 2017 by Parisot et al. (2017) for the purpose of a population-wide representation of a cohort of patients. They have since then been combined with GNNs and used on multiple medical datasets. Most works utilise population graphs as a method for multi-modal data integration (Parisot et al., 2017; Kazi et al., 2019; Cosmo et al., 2020; Bintsi et al., 2023a). Here, a subset of the features are used as node features (usually imaging features), while other features (usually non-imaging) are used to generate the graph structure (the edges).

In this work, we perform an extensive study on how GNNs are used in the context of population graphs and compare different graph learning methods to graph-agnostic baseline models. We use three benchmark citation network datasets (CORA, CITESEER, PUBMED) and five medical population graph datasets. We utilise state-of-the-art (a) static graph construction methods, (b) dynamic graph construction methods, and (c) neural sheaf diffusion models. The latter have been designed in order to address two of the most dominant problems of GNNs: over-smoothing and performance on low-homophily graphs. We investigate the usage of neural sheaf diffusion models since the graph construction methods for population graphs seem to result in unideal graph structures, which might benefit from the use of neural sheaf diffusion models.

Even though we reach comparable results to related works on population graphs with GNNs for all methods, none of the GNNs significantly outperform the strongest baseline method. This raises the question of how powerful population graphs indeed are and whether they are a suitable data representation in combination with GNNs. We conclude that currently available graph construction methods are the performance bottleneck of GNNs on population graphs compared to graph-agnostic methods. Using synthetically generated graph structures, we observe that only a nearly perfect graph structure, where almost all neighbours have the same label, results in better performance of GNNs than using the node features of the graph combined with a properly tuned non-neural network method such as a random forest or linear regression (Figure 4). Therefore the question arises whether this is possible to achieve at all. Even a dynamic graph construction method, which optimises the graph structure during training, does not reach a "good enough" graph structure. Also, models that have been designed for "low-quality" graph structures (e.g. neural sheaf diffusion models) do not improve performance on population graphs. The fact that our baseline models outperform the results reported in related works emphasises the importance of appropriate tuning of baseline methods in general and shows that the currently available graph construction methods for population graphs are not sufficient.

There are a few more graph construction methods that we did not evaluate in this work, such as *Similarity Scores*. The first one was introduced by Parisot et al. (2017) and followed by several extensions and modifications (Ghorbani et al., 2022; Vivar et al., 2021; Pellegrini et al., 2022; Peng et al., 2022; Lu et al., 2022). In this work, we focus on the usage of k-NN graphs, since this method has been shown to achieve the best results in related works (Bintsi et al., 2023b) and preliminary experiments. Furthermore, an investigation of other graph assessment metrics (Luan et al., 2021; Xie et al., 2020; Luan et al., 2022) could be interesting since homophily and CCNS are not the only metrics that quantify the quality of a graph structure.

We see two future directions for population graph studies. Either (a) new and better graph construction methods need to be developed for population graphs to bring benefits to medical downstream tasks, or (b) the usage of population graphs in combination with GNNs does not seem valuable for the performance of medical downstream tasks. For better graph construction methods we see the requirement of increasing the information content of the graph structure compared to the node features alone. This could potentially be achieved by encoding information in the graph structure that cannot be trivially added to the node features, such as genetic similarity between subjects or the risk groups in survival analysis.

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