Main Protocol

PANC-PALS Registry
PANcreas **C**onsortium for **P**rognostication, **A**dvancement, and **L**ong-term **S**trategies

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NYULH Study Number: s24-00740

Version Date: 4 November 2024

Statement of Compliance

This study will be conducted in accordance with the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), any other applicable US government research regulations, and institutional research policies and procedures. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the study participants. All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

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List of Abbreviations

AE	Adverse Event/Adverse Experience
CFR	Code of Federal Regulations
CRF	Case Report Form
CSOC	Clinical Study Oversight Committee
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
FFR	Federal Financial Report
FWA	Federal wide Assurance
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
IRB	Institutional Review Board
MOP	Manual of Procedures
N	Number (typically refers to participants)
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
OHSR	Office of Human Subjects Research
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event/Serious Adverse Experience
SOP	Standard Operating Procedure
UMC	University Medical Center
US	United States

1. Background

Pancreatic surgery research, and in turn daily practice, has seen remarkable progress as leading centers started collaborating with the aim of improving standards of care through research.(1) Although recent advances in technology have allowed collaborations of increasingly wide geographical capture, there is a long-standing history of exchange of ideas among pancreatic surgeons. Direct communication among the then thought leaders in the field paved the way for pancreatic surgery as we know it today. Anecdotally, they would often detail their experience of performing a resection on a single patient and their postoperative recovery over post mail, as was the case at the time. In a sense, these exchanges between surgeons made them pen-pals.

While a paradigm shift in the approach to research favoring collaborative efforts has been invaluable to the field, the current approaches to collaboration have limitations. These limitations are mostly two-fold, in size and in scope. Firstly, only a small number of centers are often involved in a single common project. These multicenter efforts commonly involve centers within limited geographical regions, thus diminishing the broader applicability of their findings.(2) Secondly, collaborations to date tend to focus on specific research questions, which means that both the data and conclusions drawn may lack granularity for continued research potential. As a result, multiple independent collaborations are required over time thus duplicating data abstraction efforts and study set up every time. The use of non-standardized data elements in different collaborations also impedes data transformation and unification of databases across centers. Ultimately, these limitations lead to collaborative efforts fading over time.

A global partnership is required to build a robust international registry and to lead the important work that needs to be accomplished in the field of pancreatic surgery if we are to improve the quality of care delivered to patients and their outcomes. In the case of premalignant pancreatic lesions, such as intraductal papillary mucinous neoplasms (IPMN), the fine line between curative surgical treatment versus overtreatment is a widely recognized dilemma. Individualized management and surveillance strategies for IPMN, beyond the current treatment algorithms, are needed. For malignant pancreatic lesions, surgical resection remains the mainstay curative treatment, with the potential addition of systemic therapy for those with pancreatic ductal adenocarcinoma (PDAC).(3) Although the incidence of PDAC is relatively low, 3.3% of all new cancer diagnoses in the USA, it is one of the most lethal cancers, with the lowest 5-year cancer-related survival of approximately 13%.(4) The introduction of multiagent chemotherapy regimens and therapeutic strategies have improved both median survival and cure rates as compared to surgery alone.(5) Systemic therapy is now widely used with the intent of downsizing borderline resectable and locally advanced disease preoperatively as well as to eradicate micrometastatic spread (6). Faced with a new level of complexity as the heterogeneity in disease course and oncological outcomes becomes increasingly evident, pancreatic surgery research must also progress.

The *PANC-PALS Registry,* an international multicenter registry, will be established to provide the granularity in data required for future research on new prognostic and decision support tools and advancements in the field.(7, 8) Prior experience in the field, through *The International Study Group of Pancreatic Fistula*, *The Dutch Pancreatic Cancer Group*, and *International Association of Pancreatology*, optimally equips the current team to lead this effort.

2. Objectives and Purpose

The purpose of this study is to create and maintain a research registry called the *PANC-PALS Registry*. The *PANC-PALS Registry* will generate real-world evidence of long-term outcomes after pancreatic surgery to gain a broader understanding of the implications of treatment variations in outcomes and disease course. The *PANC-PALS Registry* will provide a framework for various types of future observational research studies to be performed in the future by its members.

Every *PANC-PALS Registry* study site will have one local Principal Investigator (PI) and two Sub-Investigators. Local PIs will have the opportunity to propose future research studies focusing on prognostication of pancreatic diseases and advancement of management strategies in the field using the registry data. The *PANC-PALS Registry* will also report on global outcomes annually.

3. Study Design

3.1 Description of Study Design

This is an international multi-institutional research registry to evaluate patient outcomes. The target population of the research registry is patients undergoing pancreatic surgery for pancreatic neoplasms worldwide. The rationale for a global multi-institutional research registry is to achieve a robust dataset that overcomes the inherent limitations of single center experiences, given the relatively low volume of resectable pancreatic cancer cases at individual institutions. By pooling data from surgical centers worldwide, this research registry will facilitate more meaningful analyses of treatment patterns, surgical outcomes, and prognostic factors to advance patient care in pancreatic surgery.

The NYULH network and participating study sites utilize electronic health record (EHR) systems. This facilitates pooling of research data from study sites. Deidentified research data will be entered into a secure HIPAA-compliant research database for analysis and storage.

3.2 Information about Study Sites

Participating study sites will be identified from previous collaborative research studies, international associations of pancreatic surgeons, and international colleague networks. Participating study sites will be recruited through pancreatic surgeons interested in the *PANC-PALS Registry*. Personalized invitations will be sent to the chief of surgery/pancreatic surgery departments at pancreatic surgery centers worldwide by the PANC-PALS PI and Sub-Investigators of the NYULH study team via email to recruit study sites to the *PANC-PALS Registry*.

Participating study sites will be vetted based on volume of pancreatic resections per year (minimum 100), ability to provide data on their patient population, internal resources, and availability of a local PI. Three individuals per participating study site, including the local site PI and two investigators chosen at the discretion of the local PI, will be registered members of the *PANC-PALS Registry*.

The primary study site for the *PANC-PALS Registry* will be NYULH. As other pancreatic surgery centers worldwide agree to participate, their study site and local PI name and contacts will be recorded on an NYULH MCIT-managed network drive set up for this study and only accessible to the NYULH study team. These contact details will also be shared with the NYULH Legal team for necessary data transfer agreements (DTA).

Participating Study Site Eligibility

Eligible study sites will be very high-volume pancreatic surgery centers from various nations worldwide. A very high-volume pancreatic surgery center is defined as a medical institution or hospital performing a minimum of 100 pancreatic resections per year including all types of pancreatic resections combined, for all diagnoses. We aim to recruit and register at least 40 very high-volume medical centers from at least 4 continents (i.e. Americas, Europe, Asia, Australia/Oceania, Africa). Commitment to consecutive case submission of adult patients undergoing pancreatic resections at their institution from their initiation of participation date will be required. Participating study sites will also be expected to have the capacity to review and correct submitted data if requested to by the PANC-PALS data manager from the NYULH study site.

Primary Study Site: NYU Langone Health (NYULH)

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Participating Study Sites		
Site Name	**Country**	**Local Site PI**
1. University of Cincinnati Health	USA	Syed A. Ahmad
2. Yale New Haven Hospital	USA	Nita Ahuja
3. Baptist Health	USA	Horacio Asbun
4. University of Virginia Health	USA	Todd Bauer
5. University of Miami - Sylvester Comprehensive Cancer Center	USA	Jashodeep Datta
6. University of California, Los Angeles	USA	Timothy R. Donahue
7. Oklahoma University Health	USA	Barish Edil
8. University of Illinois Health	USA	Aslam Ejaz
9. Cedar Sinai Medical Center	USA	Cristina Ferrone
10. Mayo Clinic Arizona	USA	Zhi Ven Fong
11. Johns Hopkins Medicine	USA	Jin He
12. The University of Texas MD Anderson Cancer Center	USA	Matthew Katz
13. Emory University	USA	David Kooby
Medical University South Carolina	USA	William Lancaster

14.	University of California San Francisco	USA	Ajay Maker
15.	Piedmont Healthcare	USA	Andrew Page
16.	Stanford Cancer Center	USA	George Poultsides
17.	Massachusetts General Hospital	USA	Motaz Qadan
18.	University of Nebraska Medical Center	USA	Bradley Reames
19.	University of Alabama at Birmingham	USA	Shushanth Reddy
20.	Oregon Health and Science University	USA	Flavio G. Rocha
21.	University of Wisconsin Health	USA	Sean Ronnekleiv-Kelly
22.	Mount Sinai	USA	Myron Schwartz
23.	University of Washington	USA	Jonathan G. Sham
24.	Mayo Clinic Rochester	USA	Mark Truty
25.	Northwell Health	USA	Matthew Weiss
26.	University Hospital Cleveland Medical Center	USA	Jordan Winter
27.	UT Southwestern Medical Center	USA	Herbert Zeh
28.	Indiana University Melvin and Bren Simon Comprehensive Cancer Center	USA	Nicholas Zyromski
29.	The Royal Free Hospital NHS Trust	UK	Giuseppe Kito Fusai
30.	Queen Elizabeth Hospital Birmingham	UK	Keith Roberts
31.	Leeds Teaching Hospitals NHS Trust	UK	Andrew Smith
32.	Sahlgrenska University Hospital	Sweden	Elena Rangelova
33.	Karolinska Institutet	Sweden	Ernesto Sparrelid
35.	Skåne University Hospital - Lund	Sweden	Bobby Tingstedt
36.	Botton-Champalimaud Pancreatic Cancer Centre	Portugal	Markus Büchler
37.	Aga Khan University	Pakistan	Saleem Islam
38.	Leiden UMC	Netherlands	Bert Bonsing
39.	Erasmus MC - Rotterdam	Netherlands	Bas Groot Koerkamp
40.	Catharina Hospital - Eindhoven	Netherlands	Ignace de Hingh
41.	UMC Utrecht	Netherlands	Quintus Molenaar
42.	Seoul National University Health	Korea	Jin-Young Jang
43.	Kansai Medical University	Japan	Daisuke Hashimoto
44.	Kindai University	Japan	Ippei Matsumoto
45.	Tokyo Medical University	Japan	Yuichi Nagakawa
46.	Azienda Ospedaliero Universitaria Pisana	Italy	Ugo Boggi
47.	Pederzoli Hospital	Italy	Giovanni Butturini
48.	Universita degli Studi di Padova	Italy	Giovanni Marchegiani
49.	Humanitas Research Hospital	Italy	Alessandro Zerbi
50.	Tata Memorial Hospital	India	Shailesh Shrikhande
51.	Metropolitan Hospital	Greece	Christos Dervenis
52.	Klinikum Nürnberg	Germany	Markus Diener
53.	St. Josef Hospital - Bochum	Germany	Waldemar Uhl
54.	Ludwig-Maximilians-Universität (LMU) München	Germany	Jens Werner
55.	Institut Paoli Calmettes	France	Jonathan Garnier
56.	Helsinki University Central Hospital	Finland	Hanna Seppänen
57.	Rigshospitalet Copenhagen University Hospital	Denmark	Stefan Burgdorf
58.	The First Affiliated Hospital with Nanjing Medical University	China	Kuirong Jiang
59.	University of Calgary	Canada	Elijah Dixon
60.	Hospital Italiano de Buenos Aires	Argentina	Martin de Santibañes

4. Study Population

4.1 Inclusion Criteria

For the **RETROSPECTIVE** cohort: In order to be eligible for inclusion in this research registry, an individual must meet all of the following criteria:

- Adult patient 18-99 years of age
- Have undergone a surgical resection of the pancreas for a pancreatic neoplasm at one of the participating study sites between January of 2014 and October of 2024, including:
    - Benign, premalignant, and malignant neoplasm of the pancreas will be eligible for inclusion
    - Any surgical approach, such as open, robotic or laparoscopic will be eligible for inclusion
    - Re-resections of the pancreas in patients that have already undergone previous pancreatic surgery may also be included
    - Patients undergoing pancreatic islet cell autotransplantation concomitantly with pancreatic resection for neoplasm may also be included

For the **PROSPECTIVE** cohort: In order to be eligible for participation/inclusion in this research registry, an individual must meet all of the following criteria:

- Adult patient 18-99 years of age
- Will be undergoing a surgical resection of the pancreas at one of the participating study sites after initial IRB approval date at the participating study site (from approximately November 2024 to November 2029) for a pancreatic neoplasm, including:
    - Benign, premalignant, and malignant neoplasm of the pancreas will be eligible for inclusion
    - Any surgical approaches, such as open, robotic or laparoscopic will be eligible for inclusion
    - Re-resections of the pancreas in patients that have already undergone previous pancreatic surgery may also be included
    - Patients undergoing pancreatic islet cell autotransplantation concomitantly with pancreatic resection for neoplasm may also be included

4.2 Exclusion Criteria

An individual will be excluded from inclusion in the research registry if any of the following criteria are met:

- Patients undergoing pancreatic resections for non-neoplastic disease, such as chronic pancreatitis
- Patients younger than 18 years of age
- Patients undergoing pancreatic whole organ transplant.

4.3 Vulnerable Participants

Depending on the individual participating study site, there may or may not be any participant recruitment or direct contact with patients/participants. The participating study sites will not target inclusion of individuals that meet federal or institutional definitions of vulnerable populations.

4.4 Number of Participants

A minimum of 100 annual pancreatic resections are required per eligible study site. Following participant inclusion and exclusion criteria, 90 per year is the estimated minimum number of participants to be included per study site. The average number to participants eligible for inclusion per site is estimated to be 250.In a 15-year timeframe, between 1,350 to 3,750 participants per study site are estimated. With the recruitment of 40-60 study sites, the anticipated maximum total of participants across 60 study sites will be 225,000.

5. Study Methods and Procedures

5.1 Data Sources

Secondary clinical data (collected and to be collected as part of routine medical care) will be the main data source. Primary data sourcing may be necessary for certain data elements in some participating study sites.

For study sites already involved in other pre-existing IRB or ethics committee approved research registries or international databases such as the European Consortium on Minimally Invasive Pancreatic Surgery (E-MIPS) or national pancreatic surgery databases, they may request data transformation from their existing datasets and import into the *PANC-PALS Registry* to be done jointly by their local research team and the NYULH study team, however missing data elements may then need to be sourced from patient records or primarily in follow-up. Each study site is responsible for adhering to the protocol for the pre-existing IRB or ethics committee approved research registry or international database.

5.2 Participant Identification

The local site research team at each participating study site will be responsible for participant identification at their own study site and using their own hospital/institution EHR system. Each study site will adhere to their own institutional policies and procedures on the secondary research use of clinical data.

5.3 Data Collection

The local site research team at each participating study site is responsible for performing their own chart review and data collection.

Once eligible participants are identified, each local site participant will be assigned a unique site-specific Participant ID number (e.g., Site1 Participant001, Site1 Participant002, Site1 Participant003…). Authorized members of the local site research team will then perform a chart review using their hospital/institution's EHR (e.g., EPIC) for each identified participant to collect/record minimal necessary information needed for the conduct of this study.

The data elements to be collected from each local site participant for research purposes will be as follow:

Data domains will be outlined following the *framework for creating standardized outcome measures for patient registries (9)* into 1) characteristics, 2) treatment, and 3) outcomes (Figure 1).

1) Data elements within characteristics will further be subdivided into participant data, disease data, and provider data:
    - Participant data will include demographics (biological sex and age at time of surgery), functional baseline at presentation, past medical history, social history, family history, and germline mutation status.
    - Disease data will include presenting symptoms, workup, diagnostic investigations, biopsy/cytology, imaging, laboratory tests, and somatic mutations. Imaging data will be collected in both the reported form for specific interpretations through the eCRF as well as in de-identified file format such as DICOM files for Computed Tomography (CT) scans.
    - Provider data (to be provided by the respective study site) will include center geographic location, yearly volume of pancreatic resections, and mode of referral to tertiary center.

2) Data elements within the treatment domain will be further subdivided into type and intent.
    - Type of treatment data will include surgery and systemic treatment such as chemotherapy, radiation therapy or immunotherapy.
    - Intent will specify whether the treatment was of curative or palliative intent.

3) Data elements within the outcomes domain will include survival, disease response, postoperative complications, patient reported outcomes, and health system utilization. Loss to follow-up (LTF) will

also be included in the outcomes domain to capture final follow-up and reasons for incomplete follow-up or survival data.

5.4 Study Cohort Timeline

The *PANC-PALS Registry* will capture a retrospective cohort from January of 2014 to October of 2024 together with a prospective cohort from the date of research registry initiation for a minimum of 5 calendar years. Continuation of the research registry will be evaluated in the last quarter of 2028. The entire research registry data will be held and maintained by the primary study site, NYULH until then. If the decision is made to close the *PANC-PALS Registry* after the 5 calendar years, then the participating study sites will be allowed to retrieve their own data for institutional records before all the data held by the research registry is safely deleted.

5.5 Registry Maintenance

The *PANC-PALS Registry* will be established first at NYULH before it is officially launched to very-high volume pancreatic surgery centers worldwide. Data cleaning and reviewing will be performed by NYULH study site staff quarterly, and the participating study site PI will be contacted directly if concerns arise. There will be quarterly website updates with overview of data outcomes. Monthly newsletters will include an overview of contributed cases. Each participating study site will have (confidential) access to live summary statistics of participating study site specific outcomes (Figure 2).

6. Data Handling and Record Keeping

6.1 Data Collection and Management Responsibilities

Data collection is the responsibility of the study site staff at each study site under the supervision of the local site PI. The local site PI will be responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported at the local site level. The NYULH PI will be responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported at all study sites.

NYULH is the primary study site and will be responsible for data management of the *PANC-PALS Registry*. The *PANC-PALS Registry* database will be housed at a secure centralized encrypted research electronic data capture platform called REDCap that is managed by the PANC-PALS project managers at NYULH.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. Clinical data will be collected directly via a REDCap electronic Case Report Form (eCRF)[1] or uploaded onto the REDCap eCRF following transformation of pre-existing databases. Image data will require transfer to the NYULH High-Performance computing (HPC) system set up for the *PANC-PALS Registry.* To achieve this, the external participating study site PI and two investigators from each participating study site will be assigned unique user ID and password combinations (Kerberos computer-network authentication protocol) by NYULH to access the *PANC-PALS Registry* platform. The two local site investigators at each participating study site will be tasked with data abstraction duties.

Each site PI/study staff is responsible for knowing their institutional policies and procedures and adhering to them.

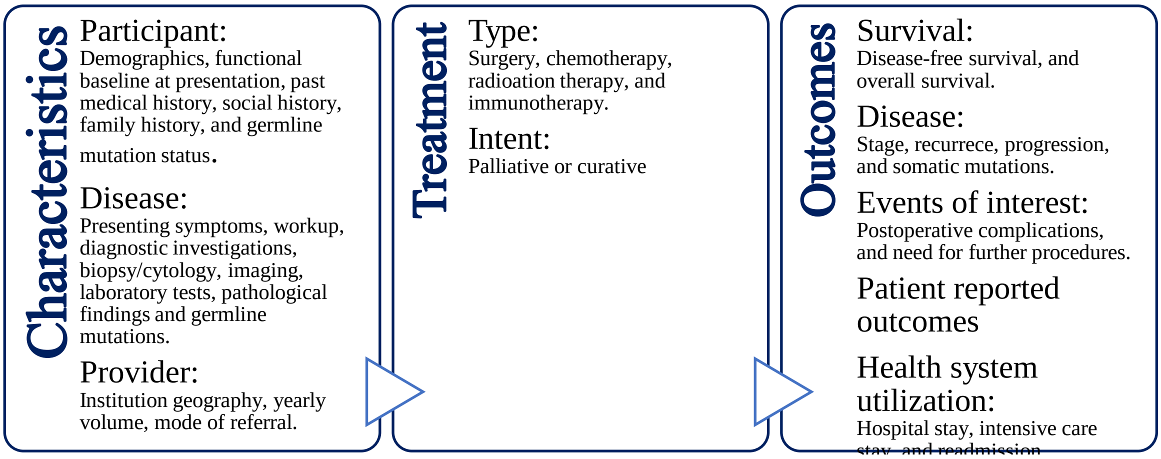

Figure 1. Summary of data elements.

To maximize internal validity, established clinical data standards will be used whenever possible. For example, outcome data elements will include standardized outcomes measures established by the International Study Group for Pancreatic Surgery (ISGPS). Standard terminology will also be incorporated into the research registry throughout all domains as extensively as possible to minimize data abstraction burden on participating study sites. The eCRF will contain the relevant summary explanations for standardized clinical data measures and terminology to aid data abstractors. Where data standards do not exist then commonly used data elements and internationally accepted data

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[1] https://redcap.nyumc.org/apps/redcap/redcap_v14.0.29/index.php?pid=114402

elements will be used instead. The NIH common data elements (CDEs) repository was examined for participant characteristics data such as race, ethnicity, sex, and baseline status. Definitions used will also be aligned with currently existing databases such as the E-MIPS to facilitate training and data abstraction process for sites. An "unknown" option will be provided for data elements that are commonly collected retrospectively from patient records to distinguish data that is not documented and missing data. Because of the international nature of the consortium, different units for laboratory tests will be allowed. The data collection tool will be pilot tested prior to launch of the research registry to ensure all data elements are satisfactory.

6.2 Data Quality Assurance

A risk-based approach to focus on the most important sources of error will be taken for data quality assurance. Errors in interpretation of data elements or coding from data abstraction will be minimized by pilot testing the eCRF for inter-rater reliability and by providing training for data collectors on definitions. Structured training will be offered to data collectors on an as-needed basis. Errors in data entry will be prevented by restricting entry fields to integers, defined number of decimal places, or letters as appropriate, by limiting ranges of values to clinically possible lower and upper limits, and by rigorous data cleaning. Errors of intention (cherry-picking cases) will be addressed by checking for data consistency between centers in similar geography and recorded center case volume as well as by performing onsite audits at random or if any concerns arise. Quality assurance concerns include missing data, incomplete cases and errors in data entry. Automated monitoring and alerts on data completeness as well as quality trending and alerting based on set thresholds (missing data >5% and >10% incomplete cases for longer than 3 months).

6.3 Data Confidentiality and De-identification

Information about participants will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and the General Data Protection Regulation (GDPR). Participant confidentiality will be held in strict trust by each local site research team. Participant medical record review will be limited to just the elements needed to complete the study.

None of the 18 patient identifiers under the Safe Harbor de-identification method for protected health information (PHI) will be collected by the *PANC-PALS Registry*. All file images to be transferred to the *PANS-PALS Registry* will be in de-identified format. This will make the *PANC-PALS Registry* a *limited dataset* as defined by the Privacy Rule. Participating study sites will assign each participant entered in the REDCap research database a unique site-specific participant ID number. Each participating study site will be required to store an encrypted electronic identifying key to the participant ID with password lock within their own institution's network or as paper copy under double physical lock be able to amend or complete their own records over time. The key to the direct identifiers will never be shared with the NYULH study site and will always remain inaccessible to the researchers analyzing the de-identified data. Health information that can be used in conjunction with other information to identify individuals such as treatment event dates or recurrence dates will be recorded as time intervals and will not be accessible to researchers performing data an analysis.

While the *PANC-PALS Registry* will solely contain de-identified patient data, through which patient's identity will not be readily ascertained, health information that can be used in conjunction with other information to identify individuals such as treatment event dates or recurrence dates will be recorded. Every attempt possible will be made by the *PANC-PALS Registry* to make indirect identifiers inaccessible to the investigators using *PANC-PALS Registry* data for future research purposes by recoding data into time intervals and uncoupling center data from all clinical data.

The investigators using *PANC-PALS Registry* data for future research purposes will thus not be able to re-identify participants nor contact patients in the *PANC-PALS Registry*.

6.4 Data Monitoring

The NYULH PI will ensure that the *PANC-PALS Registry* is conducted in full conformity with Regulations for the Protection of Human Subjects of Research codified in 45 CFR Part 46. The NYULH PI will be responsible for providing oversight of the research registry across study sites along with data monitoring at the NYULH study site.

Protocol deviations must be reported to the local IRB/ethics committee per local IRB/ethics committee guidelines. Each local site PI/study staff is responsible for knowing and adhering to their local IRB/ethics committee requirements.

The *PANC-PALS Registry* local site PIs from each participating study site and the PANC-PALS organizing scientists at NYULH will be tasked with participating study site retention duties. Retention duties will include maintaining visibility at relevant international meetings, annual outcome reports, monthly newsletters, and regular website updates. Confidential live summary graphics of institutional outcome data for each participating site will be made available to participating centers' investigators accessing the platform with their unique access codes. The main incentive for continued participation will be the ability for participating centers to publish using the PANC-PALS platform and registry data.

6.6 Dissemination of Annual Outcomes Report

Detailed dissemination of overall outcomes will be through annual *PANC-PALS Registry* report publications. Annual reports and regular updates of data contributed to the *PANC-PALS Registry* will also be summarized on the PANC-PALS website. Annual reports will include descriptive analyses of all pancreatic resections reported, treatment variations, postoperative and long-term outcomes. These will serve as regular updates of global progress in pancreatic surgery to inform clinical practice, guide further research efforts and potentially highlight knowledge gaps.

6.7 Data Ownership and Governance

Participating study sites will remain rightful owners of the data generated by their own study site and will have full access to manage their own institutional data by accessing the PANC-PALS REDCap research database with their unique Kerberos ID. The unique access codes will be assigned individually to the participating study site PI and two investigators following identity verification. Periodical password change will be required. Direct data access via unique Kerberos ID will be limited to their own study site's data.

Access to *PANC-PALS Registry* data for future research studies will require study proposal approval at the *PANC-PALS Registry* by 2/3 of *PANC-PALS Registry* local PIs at one of the registry meetings as well as confirmation of participation by other study sites that agree to participate in the approved study. Every participating study site will therefore stay in full control of the use of their own data. Wider data access for future research purposes will subsequently be provided via a dedicated data enclave restricted to prespecified data elements, length of time, and will not allow download or permanent storage outside the *PANC-PALS Registry* database.

Active members of the PANC-PALS *Registry* will be eligible to access *PANC-PALS Registry* data to perform future research studies with an emphasis on prognostication and management strategies in pancreatic surgery. Annually, at least four participating study sites will be provided prespecified access via data enclaves to analyze data for proposed research studies (Figure 3). Further details on data requests and limited access are outline in the manual of operations.

7. Ethics / Protection of Human Subjects

Approval from NYULH IRB will be obtained for setting up and management of the *PANC-PALS Registry*. Details that are specific to the local NYULH study site are available in a separate local NYULH site protocol addendum.

Local IRB or ethics committee approval will be mandatory for every participating study site wishing to partner with the *PANC-PALS Consortium* and contribute to the *PANC-PALS Registry*. Each participating study site is responsible for obtaining their own IRB or ethics committee approval before commencement of any human subjects research activities at their local study site. Each participating study site's IRB or ethics committee will have final determination on whether informed consent and HIPAA authorization are required. Each participating study site will forward their IRB or ethics committee approval to the NYULH study site.

Data use agreements will be established by the participating study sites and NYULH as the lead site after local IRB approval. The project managers at NYULH will assist individual participating study sites in this process.

PANC-PALS Registry Timeline

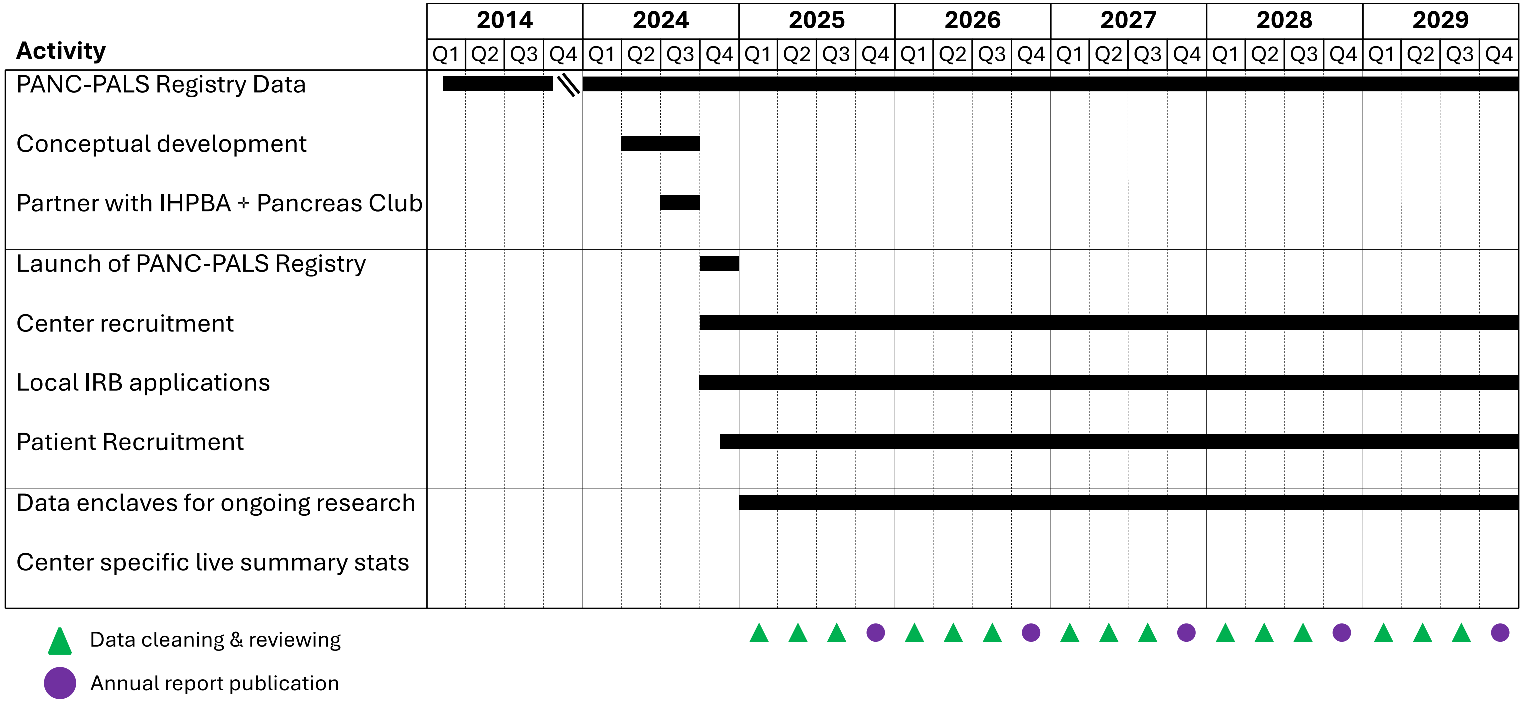

Figure 2. PANC-PALS Registry Timeline

PAN-PALS Registry Data Flow

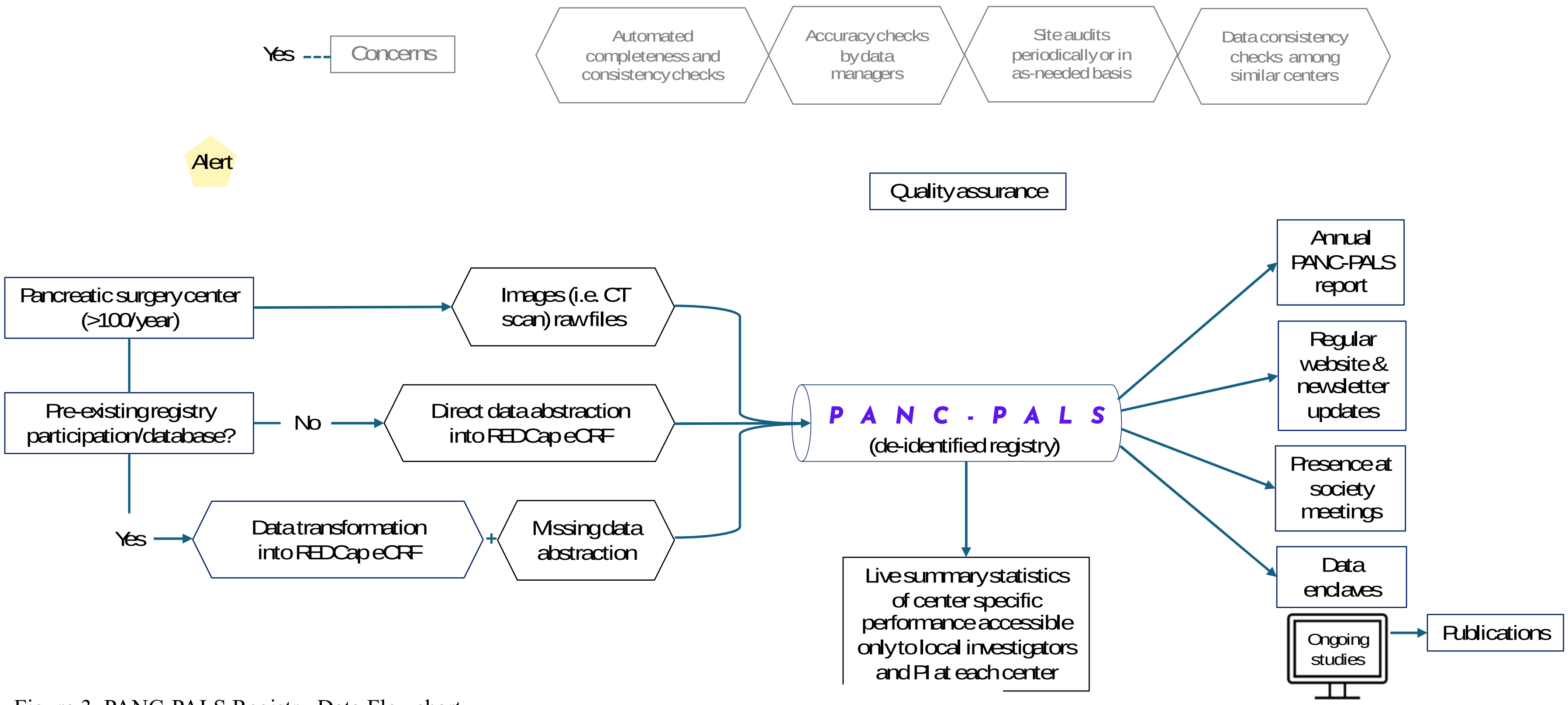

Figure 3. PANC-PALS Registry Data Flowchart

References

1. Besselink M. The Value of International Collaboration in Pancreatic Cancer Research: EURECCA. Ann Surg Oncol. 2019;26(3):705-6.
2. Jang JY, Han Y, Lee H, Kim SW, Kwon W, Lee KH, et al. Oncological Benefits of Neoadjuvant Chemoradiation With Gemcitabine Versus Upfront Surgery in Patients With Borderline Resectable Pancreatic Cancer: A Prospective, Randomized, Open-label, Multicenter Phase 2/3 Trial. Ann Surg. 2018;268(2):215-22.
3. Wolfgang CL, Herman JM, Laheru DA, Klein AP, Erdek MA, Fishman EK, Hruban RH. Recent progress in pancreatic cancer. CA Cancer J Clin. 2013;63(5):318-48.
4. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. CA Cancer J Clin. 2024;74(1):12-49.
5. Versteijne E, van Dam JL, Suker M, Janssen QP, Groothuis K, Akkermans-Vogelaar JM, et al. Neoadjuvant Chemoradiotherapy Versus Upfront Surgery for Resectable and Borderline Resectable Pancreatic Cancer: Long-Term Results of the Dutch Randomized PREOPANC Trial. J Clin Oncol. 2022;40(11):1220-30.
6. Conroy T, Pfeiffer P, Vilgrain V, Lamarca A, Seufferlein T, O'Reilly EM, et al. Pancreatic cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2023;34(11):987-1002.
7. Panni RZ, Panni UY, Liu J, Williams GA, Fields RC, Sanford DE, et al. Re-defining a high volume center for pancreaticoduodenectomy. HPB (Oxford). 2021;23(5):733-8.
8. Dreyer NA, Garner S. Registries for robust evidence. JAMA. 2009;302(7):790-1.
9. Gliklich RE, Leavy MB, Karl J, Campion DM, Levy D, Berliner E. A framework for creating standardized outcome measures for patient registries. J Comp Eff Res. 2014;3(5):473-80.