Retrospective Chart Review Studies

Designed to fulfill requirements for real-world evidence

Retrospective chart review studies are often needed in the absence of suitable healthcare databases and/or other secondary sources of information. Chart review studies facilitate the rapid collection of clinical, safety, and healthcare resource utilization (HRU) data.

Chart reviews provide tailored, patient-level datasets that are ideally suited as inputs to a wide range of burden of illness, drug utilization, safety, and health economic analyses. These studies enable you to:

- Delineate longitudinal patterns of care and HRU profiles that can be monetized
- Collect data not available in claims/administrative databases
- Evaluate associations between patterns of care and clinical outcomes of interest
- Meet EMA or FDA requirements for Post-Authorization Safety Studies (PASS)
  - Quantify and describe off-label medication use
  - Evaluate the impact of regulatory-mandated Risk Evaluation and Mitigation Strategies (REMS) and Risk Management Plans (RMPs)
- Evaluate the real-world safety profile of marketed products
- Identify unmet clinical need
- Inform clinical trial and other prospective study designs through cohort characterization and analyses of medical care variability

UBC is a partner center of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) scientific network which is coordinated by the EMA.

We are dedicated to excellence in research by adhering to the ENCePP Guide on Methodological Standards and promoting scientific independence and transparency.
## Chart data may include the following:

- Demographics
- Disease symptoms and co-morbidities
- Treatment and diagnostic history
- Treatment patterns
- Healthcare professional and emergency room visits
- Hospitalizations by length of stay and location
- Diagnostic test results
- Procedures
- Clinical and safety outcomes

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### Real-World Evidence Needs | Chart Review Opportunities

| Characterize patients and patterns of care | • Describe patient cohort and sub-groups of interest  
• Characterize usual care treatment patterns  
• Collect data void of the Hawthorne effect |
| Inform trial or registry design | • Identify care pathways  
• Quantify variability in patient characteristics and outcomes  
• Support sample size calculations |
| Identify unmet clinical need | • Describe burden of illness  
• Identify gaps in care pathways |
| Healthcare resource utilization (HRU) and estimate costs of care | • Capture HRU from medical charts to estimate direct medical costs  
• Quantify planned versus actual HRU (e.g., drug doses prescribed versus received) |
| Meet FDA/EMA risk management evaluation requirements | • Evaluate effectiveness of REMS or RMPs  
• Document (in)appropriate medication use  
• Document adherence to risk minimization measures |
| Collect clinical outcomes | • Collect patient-level data describing clinical outcomes (e.g., death, significant medical events) over time and by subgroup of interest |
| Capture and characterize safety outcomes | • Collect data on adverse and serious adverse events (AEs/SAEs), their severity, and associated management |
UBC Approach

UBC applies a proven approach to the full-service design and conduct of multinational retrospective chart review studies.

UBC’s multidisciplinary teams of epidemiologists, health economists, and outcomes researchers collaborate to tailor each chart review design. Project teams are led by managers who utilize innovative and flexible project management techniques and approaches to successfully implement these studies. Our global team of clinical research associates (CRAs) and clinical site specialists (CSSs) have local language capabilities and experience liaising with clinical sites. UBC regulatory and contract managers demonstrate in-depth knowledge of country-specific regulations and legislation.

UBC has a proprietary electronic data capture (EDC) system that is 21 CRF Part 11/EudraLex Annex 11-compliant and has been developed specifically for chart review studies.

The UBC team builds from the following areas:
- Real-world evidence solutions
- Epidemiology
- Registries and risk management
- Clinical operations
- Data management
- Analytics and biostatistics
- Pharmacovigilance
- Custom software design
The UBC approach to designing and managing chart review studies ensures that each study is:

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<th>Quality Controlled</th>
<th>Practical and Convenient</th>
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| • Designed to withstand rigor of scientific peer review  
• Employs data validations at the point of data entry  
• Enables scientifically valid chart sampling and disposition tracking | • Employs a remote monitoring model, thereby avoiding the need for costly on-site monitoring and oversight | • Facilitates site and data monitoring in real-time  
• Permits a clean dataset within days of database closure  
• Enables simultaneous data collection across multiple countries  
• Minimal burden to sites | • Employs a standard protocol and paper or electronic case report form (CRF) resulting in standardized local or multinational data |

Experience

UBC has conducted chart review studies in more than 20 countries. The studies have varied in scale from fewer than 10 sites to more than 300, with patient cohorts ranging from a few hundred to thousands. UBC has experience across a range of therapeutic areas. Studies have included evaluations of burden of illness, patterns and costs of care, mandated Drug Utilization Studies (DUS), Post-Authorization Safety Studies (PASS), and REMS evaluations.
What is UBC’s experience conducting chart review studies?

UBC offers a proven approach to the full-service design and conduct of retrospective chart review studies. Our experience in conducting chart review studies is manifested in our proven ability to design case report forms (CRFs) suited to the chart review paradigm, effectively recruit the appropriate study sites, meet ethics approval and contracting requirements, design user-friendly data capture tools, and collect robust, high quality data. UBC takes pride in the leadership we have shown in advancing chart review methodologies and operational site and project management. Our multi-disciplinary team approach combines significant scientific, clinical, biostatistical, epidemiologic, health economics, and outcomes research expertise. UBC has conducted regional and multinational chart review studies in as few as two sites to as many as 300 sites for a total of 50 to 2000 charts. UBC has experience across a range of therapeutic areas.

What are some of the countries and regions in which UBC has conducted chart review studies?

UBC has implemented chart review studies in more than 20 countries across North America, Europe, and Asia Pacific. UBC resources are strategically located in offices around the globe in order to offer global clinical operations, safety, outcomes research, health economics, and epidemiological solutions. UBC has the ability to leverage staff familiar with local market conditions, sites, and physician practice patterns for chart review programs.

Who performs the data abstraction and how are they trained?

Local site-based study staff (e.g., physicians, study nurses/coordinators) are designated and trained to perform medical chart abstraction and anonymized data entry into various data collection tools. Site-based staff is knowledgeable in the therapeutic area and familiar with the patients and their medical charts which facilitates the data abstraction process. Training is provided by UBC using detailed study manuals, data collection guidelines, and remote Web-Ex conference calls, which diminishes the need for costly on-site or centralized training sessions. For sites that would like to participate but require additional resources for data abstraction and entry, UBC can identify external data managers or research nurses who can effectively perform study-specific work.

How are sites selected?

UBC has dedicated teams focused on global site feasibility, identification, recruitment, and patient enrollment/retention which allow us to efficiently and effectively identify, qualify and enroll “best in breed” sites. To ensure study success, the aim is to identify highly committed sites with acceptable number of patient charts and the ability to provide quality data. UBC’s process begins with an initial country selection/review methodology which takes into account the complexity of the study design as well as region-specific prevalence/incidence rates for the indication of interest, availability of treatment of interest, regulatory/ethics considerations, and the competitive research landscape. The identification of potential sites is undertaken via a number of sources including the UBC Proprietary Investigator Database, Express Scripts data, literature reviews and assessment of research study databases, physician groups/patient advocacy organizations, sponsor site lists, and key opinion leaders (KOLs). The site selection process is completed with a robust feasibility process that is tailored to the protocol and study design. Based on feasibility results, the target number of sites most suited to participate in a particular chart review is selected in collaboration with the sponsor.

What is a typical chart review study timeline?

Chart review timelines generally vary from 8 to 18 months from kick-off meeting to final report/study close-out. Factors that affect timelines are the total number of study sites and chart abstractions per site, CRF complexity, per chart abstraction duration, and country-specific regulatory and ethics committee timelines. Choosing the right mix of countries and sites as well as ensuring the development of a well-thought-out protocol and CRF are paramount to study success and ensuring timelines are met.
How much country-to-country variation exists in medical charts?
The lack of standardized medical chart documentation in the usual care setting presents a challenge for any chart review study. Although reflective of actual practice, the quality of documentation can vary from country to country and potentially even from site to site within a given country. Electronic Medical Records (EMRs) have improved the quality of documentation in most cases; however, EMRs are more common in the U.S. than in other countries, therefore this improvement is not always widespread.

UBC has been successful in all studies to date by creating CRFs that streamline the data collection process and result in a standardized dataset. Generally, UBC has designed CRFs with simplicity in mind, minimizing site burden, reducing pass-through site costs and timelines, and ensuring that all variables of interest will be available at most sites. Prior to launch, principal investigators have the opportunity to review the CRF, and this feedback can be incorporated and managed proactively. UBC has not experienced a situation using this approach in which large data gaps have emerged.

How is Institutional Review Board (IRB)/Ethics Committee (EC) approval obtained and does UBC typically interact with the IRB/EC?
The guidelines for non-interventional studies are highly variable in different territories. UBC’s approach takes into consideration the type of study design and local requirements of the study sites. We assign experienced UBC staff with knowledge of local regulations to our project teams. UBC’s in-house regulatory experts maintain up-to-date intelligence and offer guidance on the processes and country-specific requirements for regulatory and IRB/EC submission/notifications as well as timeframes for review and approval. Regulatory submissions and notifications are completed centrally by our regulatory experts. The preparation of IRB/EC submissions is undertaken by local country UBC personnel, with oversight from the project manager ensuring the preparation of high quality submissions, which maximizes the likelihood of first-pass approvals.

Does UBC have expertise to manage privacy concerns and regional approvals?
Over the last decade, UBC’s research scientists, project managers, contracts managers, and regulatory experts have gathered and centralized intelligence relating to country-specific regulatory and IRB/EC requirements, contracting processes, and data privacy/protection guidelines and legislation. Collectively, our personnel have current experience to optimally design and execute studies. Protocols and CRFs are developed to comply with all data collection regulations and are completed with a view to streamline operational execution. UBC has a proven approach to rapidly starting-up study sites which begins with knowledge of the local requirements in all selected countries. We assign a multi-disciplinary team consisting of the right personnel to undertake various tasks:

• Regulatory managers provide regional guidance on the country submission needs and timelines as well as directly conduct submissions/notifications to regulatory authorities
• Contracts managers develop templates and negotiate contractual terms and conditions that are aligned with the conduct of chart review studies
• Project managers with relevant experience in data protection/privacy requirements provide input into study design and direction to the project team

Project managers identify and track all process issues and develop project-specific plans starting from study initiation. Research experience and ongoing communication with site investigators and their study nurses ensures that challenges are identified proactively and incorporated into planning.

Is it possible to pool data from several countries?
UBC is able to aggregate or disaggregate study data in any fashion. Such analyses are documented in the statistical analysis plan at the outset of each study. UBC has frequently pooled clinical outcomes across countries. Patterns of care and associated costs (i.e., health economic data) are typically not transferrable across jurisdictions because of differences in treatment practices.