FDA-ASCO: Geriatric Oncology Workshop

Leveraging research designs for real-world patients: Real-world evidence

*From RCTs to Observational Research*

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Systematic Reviews and Meta-analysis of RCTs in Geriatric Oncology

Lyman GH, Poniewierski MS: in GERIATRIC ONCOLOGY (M Extermann ed), Springer 2017 (in Press)
Systematic Reviews and Meta-analysis of RCTs in Geriatric Oncology

Number of Publications (N=61)

![Bar chart showing the number of publications by country](chart1)

Age Cut-Off Values in Publications

![Bar chart showing the number of publications by age cut-off](chart2)

Lyman GH, Poniewierski MS: in GERIATRIC ONCOLOGY (M Extermann ed), Springer 2017 (in Press)
RCTs vs Observational Data: Find the Right Balance

- Limited external validity:
  - narrow eligibility criteria (poor generalizability)
- Limited info on vulnerable subgroups:
  - elderly; comorbidities
- Feasibility and ethical issues
- Costly: time and resources
- Treatment imbalance by chance
- Limited attention to toxicities:
  - especially rare/delayed effects
  - not powered for toxicity events

The Balancing Act

- Strong internal validity
- Balanced groups
- Outcomes clearly defined
- Defined treatment alternatives
- Limited patient population
- Longer follow-up
- Strong external validity
- Real world settings
- Large sample size
- Confounded

Booth CM, Tannock IF: BJC 2014; 110: 551-555

Observational data may reflect real world experience without restrictions related to older age or major medical comorbidities
Observational Studies in Geriatric Oncology

- Breast: 6%
- Lung: 15%
- Other: 21%
- Melanoma: 1%
- Sarcoma: 2%
- Head and Neck: 5%
- Gastrointestinal: 20%
- Gynecologic: 7%
- Genitourinary: 21%

In-hospital mortality:

- All Patients: 7.3%
- Age 65-69: 6.0%
- Age 70-74: 6.9%
- Age 75-80: 7.6%
- Age 80-84: 8.5%
- Age 85+: 10.0%
- Anemia: 10.1%
- Hepatic disease: 14.3%
- Congestive heart failure: 16.2%
- Venous thromboembolism: 18.1%
- Renal disease: 20.2%
- Infection: 20.2%

n=386,377

Shayne M et al. J Geriatr Oncol 2013: 4: 310-318
The Untapped Potential of Observational Research to Inform Clinical Decision Making

Research Statement from the American Society of Clinical Oncology

Working Group

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The Untapped Potential of Observational Research to Inform Clinical Decision

PRIMARY CONCLUSION: Observational Research is Critical to Informing Health Care Decisions

• Unbiased observational studies that answer research questions of interest are complimentary to RCTs.
  • Hypothesis generating.
  • Develop evidence not answered by RCTs.

• Need to ensure the quality of observational research, as it takes on an expanded role in clinical decision making.
Recommendation 1: Establish common data standards & definitions
- National effort to promote existing and emerging standards for the collection, exchange, and reporting of digital healthcare information.
- Oncology providers should support the systematic collection of data in EMRs.
- Vendors and providers ensure products support the capture of meaningful structured data, e.g., stage, recurrence, PRO's.

Recommendation 2: Improve interoperability in electronic health records
- Legislation to ensure widespread interoperability in EMRs.
- Develop true interoperability between electronic clinical data systems.
- Ensure providers are prudent purchasers and users of EMRs.
Recommendation 3: Utilize rigorous observational research

- Follow best practices in observational research, as outlined in methodology guides.
- Training programs and professional societies provide training in interpretation and conduct of observational research.

Recommendation 4: Transparent reporting of observational research

- Encourage authors to follow reporting guidelines for observational research,
- Include experts in observational research among peer reviewers of manuscripts.

Recommendation 5: Protect patient privacy

- Identify gaps in privacy protections and ensure responsible use of observational data for research.
- Increase investment in privacy enhancing technologies and incentivize their use.
- Increase transparency about uses of patient data.
- Encourage patients’ right to access their health information.
Leveraging Observational Data to Study Novel Cancer Therapies in Older Patients

**Challenges/Opportunities**

- Linking molecular data to treatment and outcomes
- Capturing toxicities of molecularly targeted agents and immune-related adverse events
- Adjustment for major medical comorbidities
- Patient centered outcomes
  - PROs and HRQOL
  - Frailty
  - CGA
- Resource Utilization & costs

**Observational Studies**

- The Changing Landscape
- Big Data & Rapid Learning Systems
- Non-randomized controlled studies
- Cohort Studies
- Population Studies
- Cancer Registries
- Administrative & Claims Databases

**Big Data & Rapid Learning Systems**

**Cohort Studies**

**Population Studies**

**Cancer Registries**

**Administrative & Claims Databases**
Unlock, assemble, and analyze de-identified cancer patient medical records

Uncover patterns that generate knowledge

Provide guidance by identifying the best evidence-based course of care

Accelerate Innovation

CANCER LINQ: ASCO’s Big Data Initiative into Observational Data
Thank You