AXTRIA
INGENIOUS INSIGHTS

The Changing Role of Pharma Sales and Marketing in a Specialty Medicine Environment

The Changing Role of Pharma Sales and Marketing in a Specialty Medicine Environment

A Case Study of Newly Diagnosed Patients with Metastatic Breast, Colorectal, and Non-Small Cell Lung Cancer

George A. Chressanthis, Ph.D., Principal Scientist, Axtria Inc.

1. Introduction and Industry Shift to Specialty Medicines

The growing shift to specialty medicines in the US pharma market is well documented.[1] Pricing issues are becoming more common and controversial, with questions being raised about the sustainability of increasing sales revenue mainly through pricing.[2-3] Further, given the cost of newer specialty medicines, performance-based pharmaceutical pricing contracts through payers will become the norm.[4] The question this white paper addresses is simply this - what do these pharma environmental changes mean (if anything) for the future role of sales and marketing?

An important theme in the white papers and blogs published here thus far has been that companies must begin to rethink their commercial model design, supporting analytics, and data management infrastructure based on different emerging industry dynamics than seen today. Older industry dynamics included portfolios of small molecule drugs, smaller influence from payers, and lower concern over patient access/affordability. Now and going forward, project/product portfolios are increasingly being populated with expensive large molecule / biologic specialty medicines, with greater focus on personalized targeted therapies, a payer-dominated landscape, and where patient access/affordability are significant and growing concerns. The result is that the commercial model design and subsequently, the nature and role of sales and marketing must likewise shift.

2. Insights from Previous Research and Survey Work

Unfortunately, the current academic biopharma marketing science literature offers little insight into the specifics about the future commercial model design. Published works have emphasized a tactical non-strategic economic model framework myopically focused to maximize ROI of spending across various promotion channels for the purpose of increasing physician prescriptions.[5] A similar emphasis within the industry likely holds true when viewing results from an exploratory survey looking at current versus emerging sales force science issues identified as important by practitioners (e.g., people working at biopharma firms and consulting organizations).[6] Referring to **Table 1**, one can clearly see the changes from current to emerging issues in sales force strategy and operations, such as:

1. concomitant changes in analytics and big data needed (e.g., medical claims, EMR, patient-level data, digital/social media channels) to support new solutions based on health outcomes.

2. rapidly evolving environmental trends (e.g., growing influence from IDNs, ACOs, increasing consolidation between providers and payers, increasing sales rep access restrictions to physicians).

Pharma commercial analytics are currently seen mainly as a means to support tactical execution of traditional sales and marketing channels to achieve short term financial goals, rather than as a strategic asset as a key source for competitive differentiation to sustain long term industry advantage.[6] Instead, biopharma companies need to pursue a strategic open systems based approach across the entire pharmaceutical value chain throughout the project/drug lifecycle.[5] This means pharma companies will be increasingly called upon to demonstrate value through significant improvements in health outcomes and reductions in treatment costs. This latter viewpoint is consistent with a newer perspective that research-based biopharma companies must think differently

TABLE 1: Exploratory survey results on the top 2 identified current vs. emerging issues for each biopharmaceutical industry sales force science area[a]

Top 2 identified *current* (0 to 2 years out) vs. *emerging issues* (> 2 years out) for each biopharmaceutical industry sales force science area and by % of total responses.

Current Issues	Emerging Issues
1. Sales Force Strategy[b]	
21.4% Targeting quality	26.2% Institutional sales forces, especially for IDNs and ACOs
19.0% Financial outcomes	16.7% Outcomes and value-based messaging
2. Sales Force Operations[c]	
21.2% Incentive compensation	26.2% Flexible sales force deployment
16.7% Call planning	16.7% Incentive compensation
3. Sales Force Analytics	
33.3% Promotion response and ROI analytics (all channels)	16.7% Health outcomes and cost-effectiveness analyses
11.9% Marketing-mix optimization	14.3% Sales analytics that drive sales force strategy and operation outcomes
4. Big Data	
21.4% All Rx-based databases	16.7% All Rx-based databases (physician-level and product-level)
14.3% LRx (patient-level) data	16.7% Activity data from social media and digital channels
	16.7% Electronic medical records (EMR)
5. Environmental Changes	
19.0% Increasing payer influence on physician prescribing	16.7% Increased consolidation between provider and payer
14.3% Increasing sales representative access restrictions	14.3% Increasing sales representative access restrictions
	14.3% Changes in payer influence on physician prescribing

Notes:

a. Survey to industry practitioners ran 4/29/2015 to 5/22/2015 that was sent to current members and email addresses from the Pharmaceutical Management Science Association (PMSA). Survey also sent to members of the Pharmaceutical Marketing Research Group (PMRG).

b. Sales force strategy is traditionally defined as outcomes that solve for size, structure, allocation, targeting and targeting quality, sales representative-customer relationship disruption analysis, scenario planning, etc.

c. Sales force operations are traditionally defined as outcomes that solve for territory alignment, call planning, incentive compensation, objective setting, sales reporting, sales performance management metrics, etc.

Source: Chressanthis G and Mantrala M. Pharmaceutical sales force science: current and emerging trends, and issues for future research. Presentation to the Pharmaceutical Management Science Association Board. Las Vegas, NV: PMSA Annual Meeting; 17 April 2016.

and apply tools beyond traditional boundaries, while engaging in interdisciplinary-type analyses to solve increasingly more complex business problems in the future.[7]

3. Foundations Governing the Future Role and Effects of Sales and Marketing

This change in perspective likewise means traditional pharma sales/promotion response analytics has to give way to new marketing science models. These models must connect increases in the frequency and quality of sales & marketing on a different set of metrics ultimately tied to improvements in health outcomes, total treatment costs, and cost effectiveness. There are three underlying theoretical frameworks that provide the foundation for the preceding relationships:

1. Pharma sales & marketing will be designed and executed to be "*informative*", not "persuasive".[8] This foundational approach has implications for the development of the commercial go-to-market strategy and model design, and subsequent sales & marketing strategy and operations processes.

2. The growth of more complex specialty medicines will mean an increasing importance placed on the effective communication of *scientific evidence* to demonstrate value to healthcare practitioners and payers for drug adoption, formulary coverage, and patient compliance, access, and adherence.[9] This foundation will have numerous implications on commercial tactics, e.g. - sales force recruitment, training, objective setting & incentive compensation plan design, sales reporting and performance management metrics; the choice of marketing channels and the use of technology to convey complex scientific information.

3. Variations in the diffusion of medical information can create patterns of variable medical care use, which in turn, results in variations in health outcomes, expenditures (drug and treatment spending), and cost-effectiveness.[10] This foundation will fundamentally alter the approach of commercial analytics. The current approach emphasizes promotion-response of sales & marketing on physician prescription (Rx) volume creation. The future approach must demonstrate how such channels generate changes in health/economic outcomes. This means building new analytical capabilities based more on real world evidence (RWE) and health economics outcomes research (HEOR) models. This capability will be necessary to support ever-increasing managed care performance-based outcomes contracts pharma companies will need to enter to ensure formulary coverage and patient access & affordability of expensive specialty medicines.

4. Case Study Example in the Therapy Area of Anti-Cancer Drugs

4.1 Background – Why investigate anti-cancer drugs?

How then can this change in perspective be translated into practice to solve real commercial issues? We will take the emerging issue of increasing sales rep access restrictions to physicians (as previously noted in the exploratory practitioner survey) and demonstrate how to measure empirically the effects of this trend on outcomes related to newly diagnosed metastatic patients with breast (BC), colorectal (CRC), and non-small cell lung cancer (NSCLC). Can variations in sales rep access restrictions be empirically related to changes on various drug utilization metrics, and then in turn, on key outcome measures? There are a number of reasons for choosing this example as a case study:

1. The trend of increasing sales rep access restrictions to physicians has been well documented by ZS Associates through their AccessMonitor™ service.[11] Their 2016 annual report and executive summary clearly shows a continuing decline in sales rep access since 2008, with significant variations in access at both the physician specialty and geographic levels.[11] This declining access trend has significant commercial policy implications for drug companies. Oncologists are also documented as the most access-restricted physician specialty.[11]

2. Prior empirical research has shown how variations in sales rep access restrictions to physicians affect the amount and speed of physician prescription (Rx) share response. These results are consistent with theoretical expectations on the effects that increasing restrictions impose on the dissemination of new medical information events.[12]

3. Empirical research on the determinants of access restrictions affirm emerging trends identified in the practitioner survey noted earlier.[13]

4. Prior published research comments how these empirical findings affirm that suppressing the dissemination of medical information through increasing access restrictions work against the interests of physicians and patients.[14]

5. Anti-cancer drugs represent the second largest therapy class by US spending and the largest therapy area by the percentage of new drug launches.[1]

6. Keeping current with the latest information developments on anti-cancer drug R&D, clinical trials, and new novel therapies (e.g., personalized medicines, targeted cancer therapies)[15,16] by medical oncologists is challenging given the large focus biopharma companies place in this area.

7. A medical oncologist that falls behind on the latest anti-cancer drug developments can mean dire consequences to patients given the lethality of these diseases.

8. The pricing of anti-cancer drugs and assessing the value of cancer treatment options are not only present significant commercial challenges but also address key public pharmaceutical policy concerns.[17,18]

4.2 Conceptual framework – Key relationships and data elements[19]

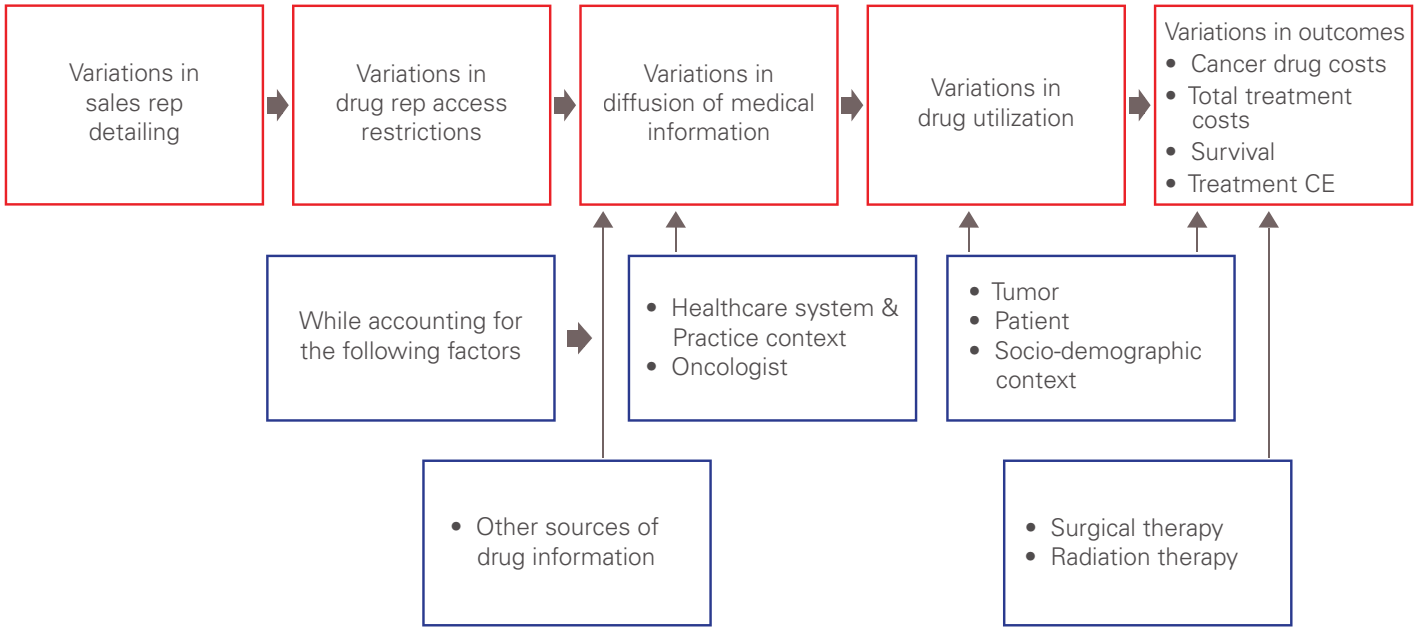
A conceptual framework on how to approach this empirical question has already been presented. **Figure 1** provides the basic relationship chain in the red boxes from variations in drug rep access restrictions to outcomes consistent with the prior three fundamental relationships. This relationship chain is supported by the evolving changes in the role and effects of sales and marketing noted earlier – principally how the dissemination of medical information affects drug utilization and in turn outcomes. The blue boxes note an example of factors along the chain that need to be accounted for to ensure proper measurement of each individual relationship outlined via the red boxes. **Figure 2** provides a more detailed conceptual framework of key relationships and specific data elements needed to measure each relationship specific for each type of metastatic cancer patient in the case study example.

The key data categories as outlined in **Figure 2** are intended to build a complete picture how sales & marketing are ultimately connected to health/economic outcomes while controlling for other key relationships, are defined follows:

- Detailing/access restrictions/drug rep access (DRA)
- Other sources of drug information
- Oncologist
- Healthcare system/practice context
- Drug utilization outcomes

FIGURE 1: Basic framework how local variations in drug rep access restrictions (DRA) affect variations in sales rep detailing, diffusion of medical information, drug utilization, and outcomes

A case study of patients with the following types of newly diagnosed metastatic cancers: breast (BC), colorectal (CRC), and non-small cell lung (NSCLC)



Notes:

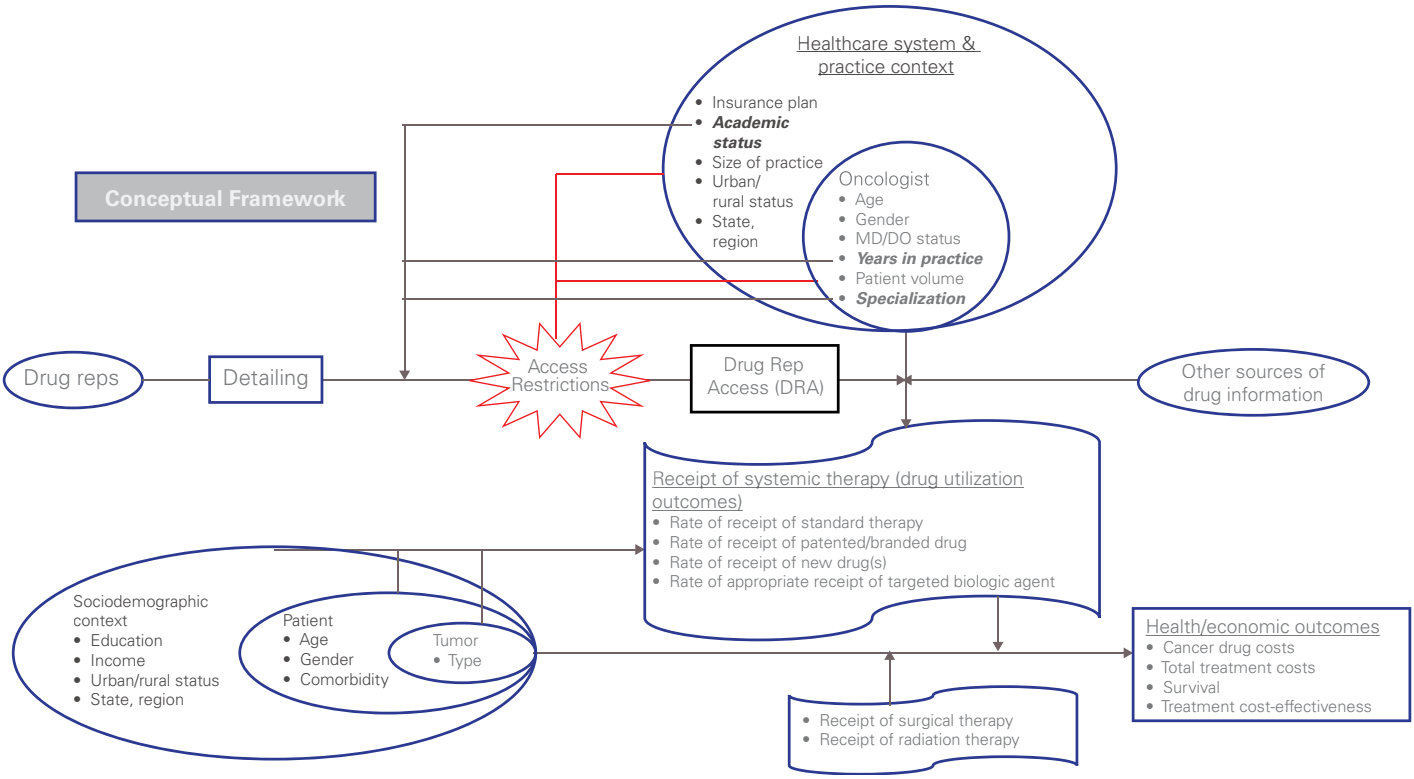
Do variations in drug rep access precede or come after variations in sales rep detailing?

- The answer depends if access restrictions are anticipated, and thus built into sales force strategy and operation planning processes (precedes), or, are viewed as unanticipated after plans are put in place (comes after). Prior empirical evidence and industry practice suggest both relationships exist.
- Some access restrictions are anticipated since pharma companies do run feasibility assumptions with the field and review call execution data on how many calls an individual oncologist will allow to be delivered prior to determining sales force strategy and operation outcomes.[13]
- Other restrictions may be unanticipated to the company caused by ad hoc administrative and/or individual physician decisions to change drug rep access.

Source: Chressanthis G and Esnaola N. Health outcome implications from restricting the flow of FDA-regulated medical information from pharmaceutical companies to physicians. Presentation at the 2015 International Health Economics Association World Congress. Milan, Italy. Session: Marketing Drugs (14 July 2015).

FIGURE 2: Detailed conceptual framework showing the relationship between variations in detailing and sales rep access restrictions to drug utilization and health/economic outcomes

A case study of patients with the following types of newly diagnosed metastatic cancers: breast (BC), colorectal (CRC), and non-small cell lung (NSCLC)



Source: Chressanthis G and Esnaola N. Health outcome implications from restricting the flow of FDA-regulated medical information from pharmaceutical companies to physicians. Presentation at the 2015 International Health Economics Association World Congress. Milan, Italy. Session: Marketing Drugs (14 July 2015).

Esnaola N and Chressanthis G. Pharmaceutical sales rep access restrictions to oncologists and cancer outcomes. NIH R01 grant proposal resubmission R01CA190551, October 2014.

- Receipt of surgical and radiation therapies
- Tumor
- Patient
- Sociodemographic context
- Health/economic outcomes

These data elements are generally available to biopharmaceutical companies through partnerships with health plans for empirical testing, and include the following:

- Nationwide patient claims database, typically contains the following segments of data by: (a) member (patient), (b) facility and professional claims, (c) pharmacy, (d) lab results, and (e) provider.
- AMA Physician Masterfile, which contains numerous physician attributes and identifying codes that allows for bridging of data files.
- US Census Data.
- National Death Index.
- Physician affiliation data, such as, Healthcare Organizational Services™ (HCOS) database from IMS Health.
- Data on sales rep access restrictions, such as AccessMonitor™ from ZS Associates.
- National Comprehensive Cancer Network (NCCN), Clinical Practice Guidelines in Oncology / NCCN Drugs & Biologics Compendia.
- US FDA Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations.
- Qualitative market research to determine the range of drug information sources and their weight of influence when oncologists make drug utilization decisions.

4.3 Conceptual framework – Modeling key relationships

The following sub-section briefly provides the basic modeling approaches required to test the significance and measure the effect of key relationships captured in **Figure 2**. A full description of the analysis plan (complete with modeling designs, empirical techniques employed, sensitivity analyses, and where appropriate accounting for missing data) for each drug utilization and health/economic outcome per cancer site has been developed.[20] DRA can be segmented into groups, using *AccessMonitor*™ access rating categories [very low (1-3), low (4-5), medium (6-7), and high (8-10)] and modeled using a multinomial logistic regression model using determinants outlined in the conceptual framework and from prior empirical research.[13] The effect of DRA on brand prescribing outcomes separately for each tumor type can then be estimated, controlling for many important factors that may confound this relationship, including oncologist factors, patient and tumor characteristics, location of treatment, and time of diagnosis. Generalized Propensity Score (GPS) based weighting with bootstrap standard errors can be used to estimate the marginal effect of DRA. Adjustments and variations on this theme can be done to measure the effect of DRA on all drug utilization outcomes).[21,22] The advantages of the propensity score-based weighting technique have been demonstrated when accounting for confounding factors, sufficient covariate overlap, and misspecification concerns.[23,24] The GPS weighted model approach can also be employed to measure the moderating effects on DRA and drug utilization outcomes from variations in oncologist and health care systems factors as noted in **Figure 2**.

The association of DRA to cancer drug costs and total cancer treatment costs per cancer site uses two methods: Kaplan-Meier Sample Average (KMSA) method[25] and an approach described by Miller & Halpern, which is similar to the Cox proportional hazard model.[26] The association of DRA to overall survival of patients with metastatic cancer per site employs the KM product-limit method to estimate the overall survival (OS) curves and the log-rank test to detect possible differences in OS among the four DRA categories, plus sensitivity and missing data tests to ensure accuracy of the estimates. Analyses on total treatment costs and overall survival per average patient per DRA category can be

combined per cancer site to determine incremental effects of changes in DRA on cost-effectiveness using statistical procedures previously noted.

5. Concluding Remarks

This white paper has tackled the questions what changes will occur and implications develop from the future role of sales and marketing in a pharma environment increasingly focused on launching specialty medicines. The case study example, while focused on the issue of increasing sales rep access restrictions to oncologists, can be adapted to address an array of other sales and marketing situations. Fundamental commercial changes are destined to happen for pharma companies in the following manner as a result of shifting project/product portfolios to specialty medicines:

1. The design and execution of sales & marketing will be increasingly directed towards *informative* promotion.
2. An increasing importance will be placed on the effective communication of *scientific evidence* to demonstrate value to healthcare practitioners and payers for drug adoption, formulary coverage, and patient compliance, access, and adherence.
3. Variations in the diffusion of medical information will create patterns of variable medical care use, which in turn, results in variations in health outcomes, expenditures (drug and treatment spending), and cost-effectiveness.

These foundational changes will fundamentally alter the strategic and operational approaches of the pharma business, shift the purpose and nature of commercial analytics requiring new capabilities and data assets, and change the organizational structure and composition of future pharma companies needed to operate successfully in this future environment focused on specialty medicines. This white paper along with previous ones on related topics provides a blue print for companies on how to prepare and operate successfully in this evolving pharma landscape.

References

1. IMS Institute for Healthcare Informatics. Medicine use and spending in the U.S.: a review of 2015 and outlook to 2020. Parsippany, NJ: April 2016.
2. Rockoff J. Pricey drugs are hurdle for new biotech CEO. *Wall Street Journal* 2016; June 7: B1-B2.
3. Walker J. Drug makers raise prices despite protests. *Wall Street Journal* 2016; July 15: B1-B2.
4. Edlin M. Performance-based pricing for pharmaceuticals. *Managed Healthcare Executive*, published online 30 September 2015, available at http://managedhealthcareexecutive.modernmedicine.com/managed-healthcare-executive/news/performance-based-pricing-pharmaceuticals?page=0,0 (accessed 22 July 2016).
5. Singh J and Jayanti R. Closing the marketing strategy-tactics gap: an institutional theory analysis of pharmaceutical value chain. In: Ding M, Eliashberg J and Stremersch S. (eds.) *Innovation and marketing in the pharmaceutical industry: emerging practices, research, and policies*. New York: Springer, 2014, pp. 710-735.
6. Chressanthis G and Mantrala M. Pharmaceutical sales force science: current and emerging trends, and issues for future research. Presentation to the Pharmaceutical Management Science Association Board. Las Vegas, NV: PMSA Annual Meeting; 17 April 2016.
7. Castellani J. Keynote presentation: The changing healthcare environment. Pharmaceutical Management Science Association Annual Conference 2015. Presentation on April 20, 2015, Arlington, VA.
8. Rod M and Saunders S. The informative and persuasive components of pharmaceutical promotion. *International Journal of Advertising* 2009; 28: 313-349.
9. Azoulay P. Do pharmaceutical sales respond to scientific evidence? *Journal of Economics & Management Strategy* 2002; 11: 551-594.
10. Phelps C. Diffusion of information in medical care. *Journal of Economic Perspectives* 1992; 6: 23-42.
11. Khedkar P and Sturgis M. *AccessMonitor*™ and *AffinityMonitor*™ 2016 executive summary: want better access to physicians? Understand what's top of mind. Evanston, IL: ZS Associates, August 2016.
12. Chressanthis G, Khedkar P, Jain N, et al. Can access limits on sales representatives to physicians affect clinical prescription decisions? A study of recent events with diabetes and lipid drugs. *Journal of Clinical Hypertension* 2012; 14: 435-446.
13. Chressanthis G, Sfekas A, Khedkar P, et al. Determinants of pharmaceutical sales representative access limits to physicians. *Journal of Medical Marketing* 2014; 14: 220-243.
14. Chressanthis G, Khedkar P, Jain N, et al. Suppressing commercial speech is not in the best interest of physicians and patients. *Journal of Clinical Hypertension* 2013; 15: 219-220.
15. Ingelman-Sundberg M. Personalized medicine into the next generation. *Journal of Internal Medicine* 2015; 277: 152-154.
16. Shih Y, Smieliauskas F, Geynisman D, et al. Trends in the cost and use of targeted cancer therapies for the privately insured nonelderly: 2001 to 2011. *Journal of Clinical Oncology* 2015; 33: 2190-2196.
17. Howard D, Bach P, Berndt E, et al. Pricing in the market for anticancer drugs. *Journal of Economic Perspectives* 2015; 29: 139-162.

18. Schnipper L, Davidson N, Wollins D, et al. American society of clinical oncology statement: a conceptual framework to assess the value of cancer treatment options. *Journal of Clinical Oncology* 2015; 33: 2563-2577.

19. Chressanthis G and Esnaola N. Health outcome implications from restricting the flow of FDA-regulated medical information from pharmaceutical companies to physicians. Presentation at the 2015 International Health Economics Association World Congress. Milan, Italy. Session: Marketing Drugs (14 July 2015).

20. Esnaola N and Chressanthis G. Pharmaceutical sales rep access restrictions to oncologists and cancer outcomes. NIH R01 grant proposal resubmission R01CA190551, October 2014.

21. Imbens G. The role of the propensity score in estimating dose-response functions. *Biometrika* 2000; 87: 706-710.

22. Spreeuwenberg M, Bartak A, Croon M, et al. The multiple propensity score as control for bias in the comparison of more than two treatment arms: an introduction from a case study in mental health. *Medical Care* 2010; 48: 166-174.

23. Austin P. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behavorial Research* 2011; 46: 399-424.

24. Drake C. Effects of misspecification of the propensity score on estimators of treatment effect. *Biometrics* 1993; 49: 1231-1236.

25. Lin D, Feuer E, Etzioni R, et al. Estimating medical costs from incomplete follow-up data. *Biometrics* 1997; 53: 419-434.

26. Miller R and Halpern J. Regression with censored data. *Biometrika* 1982; 69: 521-531.

George A. Chressanthis, Ph.D.
Principal Scientist
Axtria Inc.
300 Connell Drive, Suite 5000
Berkeley Heights, NJ 07922
Email: george.chressanthis@axtria.com

Contact Us

+1-877-9AXTRIA
insights@axtria.com

Disclaimer

Axtria® understands the compliance requirements behind personalization and we do not work with any personally identifiable data that can identify an end-customer of a business.

We have the strictest data security guidelines in place as we work with businesses to improve the experience for their customers.

www.axtria.com
facebook.com/AxtriaInc/
insights@axtria.com
linkedin.com/company/axtria
@AxtriaConnect

Founded in 2010, Axtria is a global provider of cloud software and data analytics to the Life Sciences industry. We help Life Sciences companies transform the product commercialization journey to drive sales growth and improve healthcare outcomes for patients. We continue to leapfrog competition with platforms that deploy Artificial Intelligence and Machine Learning. Our cloud-based platforms - Axtria DataMAx™, Axtria SalesIQ™, Axtria InsightsMAx™ and Axtria MarketingIQ™ - enable customers to efficiently manage data, leverage data science to deliver insights for sales and marketing planning, and manage end-to-end commercial operations. We help customers in the complete journey from Data to Insights to Operations.

For more information, visit www.axtria.com

Follow Axtria on Twitter, Facebook and LinkedIn