# Statistics in Epidemiology: Communication is the Key to Success

Jashvant Poeran MD PhD<sup>1</sup>, Nicole B. Valentine MA MPH PhD candidate<sup>2</sup>, Gouke J. Bonsel MD PhD MPH<sup>3</sup> Ann Zauber PhD<sup>4</sup>, Jason H. Moore BS MA MS PhD<sup>5</sup> <sup>1</sup>Assistant Professor, Institute for Healthcare Delivery Science, Department of Population Health Science & Policy, Icahn School of Medicine at Mount Sinai, 1425 Madison Avenue (Box 1077), New York, NY 10029 <sup>2</sup>Health Economist and Technical Officer, Secretariat member of WHO's former Commission of Social Determinants of Health, Department of Public Health, Environmental and Social Determinants of Health, World Health Organization, Geneva, Switzerland <sup>3</sup>Professor of Perinatal Care and Public Health, Department of Obstetrics and Gynecology / Public Health, Erasmus Medical Center, Rotterdam, The Netherlands <sup>4</sup>Attending Biostatistician, Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY, United States <sup>5</sup>Professor of Genetics, Professor of Community and Family Medicine, Director of the Institute for Quantitative Biomedical Sciences, Associate Director, Norris-Cotton Cancer Center (NCCC), Dartmouth-Hitchcock Medical Center, Lebanon, NH

#### Abstract

Statistics in epidemiology can serve as a goal itself but can also serve as a means to create awareness among policymakers. An important part of this is effectively communicating the statistics to not only these policymakers but also, e.g., healthcare personnel and lay audiences. In topic-contributed session #389 speakers from different backgrounds have discussed examples of effective communication of statistics in epidemiology, and provided some tips and tricks on effectively creating awareness study results. This manuscript provides a brief overview of the most important lessons learnt through speakers' experiences.

**Key Words:** Epidemiology, Communication, Policymakers, Health Systems, Perinatal Care, Cancer Screening, Visualization Software

#### **1. Introduction**

Topic-contributed session #389 featured four presentations on speakers' experiences regarding effective communication of statistics in epidemiology. These statistics can serve as a goal but can also serve as a powerful means to create awareness among policymakers. An important measure of successful communication is effectively communicating the statistics to not only these policymakers but also, e.g., healthcare personnel and lay audiences. During this session examples of effective communication of statistics in epidemiology were discussed. Moreover, speakers provided tips and tricks on effectively creating awareness of study results that -most importantly- could eventually lead to healthcare practice improvements and future funding. To achieve a broad view on

successful strategies speakers were selected from different backgrounds with their presentations ranging from international comparison of health systems' responsiveness, and information visualization methods to informing policymakers on optimal models for cancer screening.

This article will provide a brief background and summary of the most important conclusions from each of the four presentations. The order in which the presentations were given during the session will be maintained.

### 2. Reporting health systems responsiveness and patient-centred care: lessons for making qualitative information a spur for action

Nicole B. Valentine: valentinen@who.int

Qualitative information has some unique challenges for communication to health policymakers. Unlike with physical phenomena that can be counted (mortality, health workers) or diagnosed (cause of disease), qualitative information suffers from lack of tangibility, and, therefore, threats to comparability in the form of "subjectivity", difficulty in measuring causal pathways, and in identifying improvements over time. Research for qualitative information in the health sciences does not typically attract large funding, making it still harder to address systematically. Experiences of measuring and communicating 'Health Systems' Responsiveness' in the international context, albeit a qualitative construct that was "quantified", are instructive for thinking about how to approach the communication of qualitative information to policymakers more generally. Responsiveness is a latent construct providing information on quality of care from the user's or prospective user's perspective along a set of 8 domains: Autonomy, Communication, Confidentiality, Dignity (respect for persons); Choice, Prompt Attention, Quality of Basic Amenities, and Social Support (access to) (client orientation).

The Responsiveness construct and its measurement approach was developed and brought to policy-makers' attention internationally by WHO largely between 1999-2003 as part of the health systems performance assessment evaluation framework.<sup>1</sup> Responsiveness added a qualitative, and human rights dimensions to the care process and outcomes, apart from population health and the fairness in financing, which were also measured in the health systems performance framework. The measurement approach adopted was to have strong explicit, clearly stated measurement steps, each connected to statistical criteria that were discussed with policy-makers. The measurement steps included certain traditional approaches and other more innovative ones. Among the more traditional approaches in other fields, although less standardized in health systems research at the time, were: (a) to interview users of health services (inpatient/outpatient) rather than the general population's and to focus questions on their actual experiences within a defined time period; (b) to minimize overlap with health and financial protection by focusing on other mechanisms important to the well-being of people, for example: the efficient use of time for physical access, may hinder completion of treatment<sup>2</sup>; and (c) to ensure that numerical values were assigned to score users' experiences. An innovative statistical procedure was introduced for adjustment of the latent scale for reporting behaviour shifts dependent on different use of language or expectations. Explicitness with regard to complicated technical procedures to a non-technical audience was not always rewarded with understanding or acceptance, and this sometimes led to misunderstandings but it was nevertheless essential to the process.<sup>3</sup>

Yet, once these basic technical features of the measurement approach had been broadly accepted, other features of description of the measurement approach and presentation of results played an important role in communication and ultimate uptake. These other features have been grouped under the following paraphrased questions policy-makers would ask themselves: (1) who in my constituency cares about it? (2) who is doing better or worse than me? (3) what impact is it having on other tangible things I care about? In response to question (1), social validity is extremely important for non-tangible phenomena. A simple visual chart showing the percentage of the population ranking responsiveness' importance relative to health or financing was used effectively in many cases to respond to this query. Also, while much technical research can be undertaken to verify latent variable characteristics (e.g. intra and inter-item reliability), a simple ranking of the population's responses to direct questions on the importance of responsiveness domains immediately raises interest levels more acutely, than, say, factor analyses. In response to question (2), defining acceptable and, more importantly, unacceptable levels of performance, which can be done quite simply through illustrative stories or vignettes, was found to be very important for making the Responsiveness more tangible and actionable. For example it may be conceded that any persons returning from a health sector encounter and indicating that "medical explanations of the treatment were given, but they do not know why the treatments was needed and were worried" is an unacceptable level of quality of health care provision. Few would counter this, either from a medical point of view, because patients who understand less are likely to be less compliant, or from an ethical and compassionate perspective. The statistical models underpinning this analysis are complicated regardless of whether they are parametric or nonparametric, but results can be communicated quite accurately and effectively with these types of reference stories. Also in response to (2), "compare, compare, compare" should be the mantra for latent variables. Sensitive issues to capture policy interest for responsiveness at the time were outpatient health services versus inpatient hospital (financial/budgeting sensitivity, and medical referral sensitivity); private versus public (legislation); and different population groups and geographic regions in the country that could be ranked by wealth or health outcomes (equity).

Finally, in considering question (3) after the fact, it could be true to say that not enough was done at that time to describe the relationship between Responsiveness and health service coverage. Policy-makers in particular in health feel accountable for how well services are reaching populations in need. Therefore, associative comparisons of Responsiveness with health coverage rates, while not the main point of the Responsiveness, could have strengthened the case for monitoring responsiveness.<sup>4</sup> But at the time when it was critical to capture policy-maker's attentions, the survey design did not allow for longitudinal data gathering to assess causative relationships. Perhaps a lesson to be drawn from this is that at the outset, investment in both cross-sectional and longitudinal surveys is more important for communicating qualitative information.



#### Figure 1 (Source: World Health Survey 2002-03 example country data)

Users of health services from poorer households generally experience more problems than their wealthier counterparts; in particular this difference is notable for involvement in decision-making in both ambulatory and inpatient services, and for access to, and waiting times in, ambulatory (outpatient) health services. Wealthier patients report more access and waiting problems in relation to hospital services; but this unexpected finding may be due to their having higher expectations of the speed of access to services. In the end, with modest communication efforts along the lines described above, Responsiveness did find traction in some countries' national health plans and strategies. These and other efforts by national quality of care research agencies or intergovernmental bodies have meant it remains a feature of health systems performance internationally, but Responsiveness remains an under-monitored and under-reported construct in most health systems.

National public health institutions supporting Responsiveness types of quality of care research continue to look for ways to ensure a sustained monitoring approach is found, by using the simple approaches outlined above, as well as more sophisticated economic arguments (e.g. costs of discharge against medical advice). Finally, it is worth considering that by virtue of it being less tangible, and therefore less verifiable, if approaches to responsiveness measurement is not standardized and done routinely by non-partisan groups, its use can be abused by interest-groups wishing to dis-inform or confuse the public and health care providers. This danger can only be avoided if investments are made in both monitoring Responsiveness and ensuring clear communication of results.

# 3. Connecting statistics to national and regional policy: healthcare during pregnancy and birth

Gouke J. Bonsel: g.bonsel@erasmusmc.nl

For long, Dutch authorities and caregivers alike assumed the Dutch perinatal care (care around pregnancy and birth) system to perform superior both in terms of absolute performance (low perinatal morbidity and mortality rates) and in relative performance (little inequalities according to socioeconomic status, migrants status, living place, and hospital/midwife care organization). The first evidence to the contrary, was underestimated and perhaps wrongly interpreted and explained the status of perinatal care in The Netherlands by high maternal age, high twin rate, and smoking during pregnancy, while the rate of interventions during pregnancy (cesarean section, epidural analgesia, induction of labor) were claimed to be too high and perhaps itself a source of poor performance.

Three consecutive reports from the European perinatal outcome observatory ('PERISTAT') with data from 2000, 2004, and 2008 proved otherwise: perinatal mortality and related parameters showed The Netherlands consistently to rank among the worst performing EU-countries.<sup>5</sup> Results were confirmed in detailed national analyses and additional material on deep inequalities at the local urban and national level.<sup>6</sup> Evidence emerged on an important role for the midwife/gynecologist based system and poor 24/7 performance (i.e., inequalities in quality of care related to outcomes outside of office hours).<sup>7</sup>

The public, professionals and politicians called for a change focusing on organizational integration of midwifery practices and hospitals, on risk management, and focused care of the deprived populations in urban areas. However, at that stage analyses on modifiable factors were in its infant stage, without evidence on the relative role of individual patient risk factors, living place effects ('neighborhood': social, physical environment), and various aspects of professional (healthcare) performance. Over the course of years we introduced a set of concepts and associated analytical and presentational formats to prioritize improvement programs and to monitor progress thereof.

The first concept was the reproductive cycle: by genetics, epigenetics, and unchanged externalities the adverse outcomes tend to 'reproduce themselves'; hence, it is critical to intervene in this chain. This implies a focus on high-risk groups, i.e. women with previous adverse pregnancy outcome, or pregnant women themselves being born with perinatal morbidity.

The second concept was to split perinatal mortality in a (preceding) morbidity part, a case fatality part ('what rate of perinatal morbidities actually dies'), and a set of risks and health service effects exerting influence on the various probabilities for an adverse course (see Figure 2).

It appeared only 4 morbidities ('Big4'), all of them amenable to prevention and/or improvement, precede mortality: congenital anomaly, premature birth (before 37 weeks of gestation), small for gestational age (a birth weight below the 10th percentile), and a low Apgar score, in particular if coinciding.<sup>8</sup> From here we introduced systematic screening for 'Big4' risk factors during the first visit to a caregiver during pregnancy to lower Big4 incidence, and various measures to improve delivery to lower case fatality rate.

The screening rested on the so-called 'risk accumulation' concept, assuming that clinical and non-clinical factors alike add to the Big4 risk, and should simultaneously be addressed. This concept assumes the accumulation of non-critical risks above a threshold to be more relevant than conventional single-high-risks, and was successful in explaining existing datasets.<sup>9</sup> To that purpose screen outcome was returned to the patient as preventive and curative suggestions based on guidelines embedded in the Electronic Medical Record system.

On the macro-level we introduced a new multilevel approach for attributable risk estimation, where in our case 3 levels of aggregation matter (individual, hospital, neighborhood/city) and where considerable collinearity is present. It showed that if organizational factors (e.g., hospital staffing levels outside office hours) are - conventionally- treated as left over, their contribution to explain perinatal mortality is 7% where it is 34% if regarded the primary factor in analysis.<sup>10</sup> The individual socio-economic and ethnicity variables showed strong interaction in their effect on adverse outcome. In current research we aim at further specification of social effects (individually, living area) and organizational effects (risk management, instrumental policy, travelling distance, hospital size, etc.). Together, these analytical tools connected to specific intervention and improvement programs have changed the perinatal mortality enigma into manageable topics.

Parallel to analysis, we started a communication policy of concepts and quantitative results. The most important communication tool was the use of maps, depicting crude and standardized risk factor prevalences, morbidity incidence, and case-fatality and mortality rates. We systematically applied standardization of outcomes on local, regional, and setting (hospital) level, combining unadjusted and adjusted data, direct and indirect standardization and different reference populations. Moreover, we developed a new format by indirect standardization ('how well do you perform, if we compare you results to those of other units/places when we assume the other units have your population'). This standardization of the other units, rather than the one under study, apparently focus stakeholders best on their own challenge to improve.

Overall, 5 lessons were learnt in quantitative research in multilevel public health challenges:

- 1. A conceptual model with easy-to-understand terms highly facilitates both science and communication and policy development.;
- 2. Chronological relations for the sake of communication must be cautiously presented as causal relation;
- 3. Overarching risk concepts and risk-relation concepts (sum scores, rankings, relative risk, attributable risk, deaths/diseased avoided);
- 4. Medical risks, non-medical risks, health service risks should be treated equally;
- 5. Maps with crude and tailored standardized communicate best.



# Figure 2A

Overview of our concept of 1) the pregnancy cycle (middle), 2) proposed factors affecting (left), and 3) targets for interventions (right).



#### Figure 2B

Graphical overview of the comparison of standardized measures of outcome (e.g. perinatal mortality) and patient (e.g., ethnicity) and neighbourhood (e.g., deprived neighborhood) determinants between two neighborhoods. Neighborhoods are located in Rotterdam, the second largest city in The Netherlands.

# 4. Decision Analysis of Colorectal Cancer Screening Tests by Age to Screen, Age to End Screening, and Screening Intervals

#### Ann G. Zauber: zaubera@mskcc.org [work supported by U01 CA 152959]

Colorectal cancer (CRC) is the second leading cause of cancer in the United States. However, CRC deaths can be prevented by screening. In the 1990's three randomized controlled trials demonstrated that a guaiac based fecal occult blood test (FOBT) reduced colorectal cancer mortality from 15 to 33% (depending on the test and the interval of rescreening). Since then we have had four randomized controlled trials demonstrating that flexible sigmoidoscopy screening also reduces CRC with publications of 2010, 2011, 2012, and 2014.<sup>11-14</sup> Randomized controlled trials of screening colonoscopy are in progress.<sup>15</sup> Also, new screening tests have been introduced such as multi-target stool DNA.<sup>16</sup>

The United States Preventive Services Task Force (USPSTF) provides periodic recommendations on screening. Their decisions are based on a detailed systematic review of the literature. In 2002 in recognition of the evidence from the FOBT randomized trials, they recommended screening for CRC in asymptomatic individuals but said there was insufficient evidence to recommend one test over the other. In 2008 the USPSTF wanted to update these recommendations but realized that there would not be randomized controlled trials in the literature on what age to begin, end, and intervals of screening. For the first time they requested a decision analysis of the age to begin (age 40, 50, or 60), age to stop screening (age 75 or 85) and intervals of screening (5, 10, 20 years for endoscopy and 1, 2, or 3 years for FOBT). The screening tests considered were colonoscopy, flexible sigmoidoscopy with and without accompanying FOBT, FOBT only (fecal immunochemical test or guaiac based). The Cancer Surveillance and Intervention Modeling Network (CISNET) for CRC conducted this analysis.

The CISNET model for colorectal cancer has a natural history model of the adenomatous polyp being the precursor lesion for CRC. Some CRC screening tests can only detect a CRC and some can detect the adenoma or at least advanced adenomas as well as a CRC. The CISNET model 'microsimulates' a population at risk with respect to the adenomacarcinoma natural history; the model then repeats the microsimulation with a screening intervention on the natural history model to determine how many life years gained with screening is obtained with different screening tests. The USPSTF always weighs risks to benefits in its recommendations. Given that the USPSTF does not consider costs, the risk scale is based on the number of colonoscopies required to screen with a given strategy where the number of colonoscopies represents resource use as well as risk of complications of colonoscopy such as perforation or major bleeding.

The results for the colonoscopy strategies for age to begin, stop (end), and intervals of screening are shown in Figure 3. The more intensive the screening strategy the more life years are gained but also the number of colonoscopies for the more intensive strategies also increases. However there are few additional life years gained in going from a screening strategy of beginning screening at age 50 and stopping at 75 and stopping at age 85 with 10 year intervals but there are additional colonoscopies with little added benefit. This finding of balance for life years gained and resources required was similar for the other screening tests considered. The USPSTF recommendation for asymptomatic average risk individuals was for ages 50 to 75 to conduct screening with high sensitivity

FOBT, flexible sigmoidoscopy with FOBT, or colonoscopy (Grade A); for ages 76 to 85 do not screen routinely (Grade C), and for those over 85, do not screen at all (Grade D).

These USPSTF recommendations were well received with a positive editorial on the synthesis of the evidence review and the decision analysis by the CISNET microsimulation modeling. However, papers were soon questioning these recommendations. The recommendation of start at age 50 and continue until age 75 meant that a subject had had consistent negative screening with no findings of adenomas or colorectal cancer. However, there was a misunderstanding in the general medical community that this meant someone age 76 with no prior screening would not need to be screened at all. This example emphasizes not only the importance of communication but also the challenge of thinking about how your study results will be interpreted. To correct this misunderstanding we did a new analysis using the USPSTF task force analytical approach but with for those with no prior screening for those ages 76 to 90. We considered at least one screening of colonoscopy, flexible sigmoidoscopy, or a fecal immunochemical test at age 76 up to age 90. In this analysis we now included cost (of screening, complications, and treatment) and different life expectancies given different levels of comorbidity.

The new analysis first determined that CRC screening for elderly subjects over 75 with no prior screening was effective in providing life years gained with screening. However this effectiveness of CRC screening in unscreened elderly persons declined with increasing age and by age 90 there was even net harm. The age to which screening should be considered declined by the presence and severity of other comorbidities in the patient; up to age 86 for those with no comorbidity, up to age 83 with moderate comorbidities, and only up to age 80 for those with severe comorbidities. Also, colonoscopy as the screening of choice would stop three years earlier than the maximum stopping age per comorbidity; i.e. stop any screening at age 86 for those with no comorbidities but colonoscopy is the screening test of choice only up to age 83. This new analysis provided further guidance for ages to stop screening based on comorbidity and prior screening exposure.



--- Frontier of efficient strategies (40, 50, 60 y)

# Figure 3 (Source: Zauber et al. Ann Intern Med 2008;149:659-669)

Life years gained per 1000 persons screened by number of colonoscopies required per strategy. This example is for colonoscopy as the screening test. Each point represents a screening strategy of age to begin, age to end, by interval of repeat screening. For example '50-75,10' represents begin screening at age 50 and continue to age 75 with repeat screening at 10 year intervals for colonoscopy at ages 50, 60, and 70. Those with adenomas or colorectal cancer detected during the screening would be referred for surveillance colonoscopy and no longer be part of the average risk screening population.

# 5. Intuitive Visualization of Statistical Epidemiology Results

Jason H. Moore: jason.h.moore@dartmouth.edu

Communication of data, data analysis results and knowledge is critically important in biostatistics and epidemiology. Visualization is central to this effort. We make the distinction here between information visualization, scientific visualization and an emerging discipline called visual analytics. Information visualization is the discipline of representing data visually as scatterplots, bar graphs and heat maps, for example.<sup>17</sup> This is in contrast to scientific visualization that is defined as the computer science, engineering and physics behind representing visual information on a display such as a computer

monitor. While information visualization and scientific visualization are key components of any communication strategy, they are both greatly enhanced by technology such as gesture computing that facilitates human-computer interaction (HCI) and the integration of statistical analysis into visual representation. It is the combination of these methods and their close coordination that is now referred to as visual analytics.<sup>18</sup>

The challenge for the near future is to integrate and exploit emerging technologies that will greatly enhance the power of visual analytics for communication. For example, video game technology is a huge driver of innovation in the computer hardware market and has become an integral part of the formative years of many scientists. Current and future generations of scientists are and will be very comfortable with video games. As such, we should harness video game engines to develop visualization applications that much more closely resemble video games in their look and feel. Indeed, several data analysis software packages have been developed using video game engines. Moore et al. developed a 3D heat map for interactive visualization and analysis of human microbiome data using the Unity 3D video game engine.<sup>19</sup> Using Unity 3D for visualization has also been explored by Lv et al.<sup>20</sup> The advantage of video games is that are inherently interactive with advanced tools for animation, sound and human-computer interaction. The science community is behind the curve on integrating these technologies into biomedical research. It is our prediction that advances in this area will greatly impact research and the communication of research results to other researchers and to patients and the public.

#### Acknowledgements

The session panelists would like to thank Dr. Allen H. Heller, MD for chairing the topic-contributed session.

#### References

- 1. Murray, C. J., & Frenk, J. (2000). A framework for assessing the performance of health systems. Bulletin of the World Health Organization, 78(6), 717-31.
- 2. McIntyre, D., Thiede, M. & Birch S. (2009). "Access as a policy-relevant concept in low- and middle-income countries." Health Economics, Policy and Law, 4, 179-193.
- 3. Anand, S., W. Ammar, T. Evans, T. Hasegawa, T. Kissimova-Skarbek, A. Langer, A.O. Lucas, L. Makubalo, A. Marandi, G. Meyer, A. Podger, P. Smith, and S. Wilbulpolprasert 2003. "Report of the Scientific Peer Review Group on Health Systems Performance Assessment". In Health Systems Performance Assessment: Debates, Methods and Empiricism, edited by C.J.L. Murray, and D. Evans, pp. 839-916. Geneva: World Health Organization.
- 4. Valentine, N., Prasad, A., Rice, N., Robone, S., & Chatterji, S. (2009). Health systems responsiveness: a measure of the acceptability of health-care processes and systems from the user's perspective. In P. C. Smith, E. Mossialos, I. Papanicolas, & S. Leatherman (Eds.), Performance Measurement for Health System Improvement (pp. 138-186). Cambridge University Press.
- 5. Buitendijk SE, Nijhuis JG. High perinatal mortality in The Netherlands compared to the rest of Europe. Ned Tijdschr Geneeskd 2004. 148:1855-60.

- 6. de Graaf JP, Steegers EA, Bonsel GJ. Inequalities in perinatal and maternal health. Curr Opin Obstet Gynecol. 2013;25(2):98-108.
- de Graaf JP, Ravelli AC, Visser GH, Hukkelhoven C, Tong WH, Bonsel GJ, Steegers EA. Increased adverse perinatal outcome of hospital delivery at night. BJOG. 2010;117(9):1098-107.
- 8. van der Kooy J, Poeran J, de Graaf JP, Birnie E, Denktasş S, Steegers EA, Bonsel GJ. Planned home compared with planned hospital births in the Netherlands: intrapartum and early neonatal death in low-risk pregnancies. Obstet Gynecol. 2011;118(5):1037-46.
- 9. Timmermans S, Bonsel GJ, Steegers-Theunissen RP, Mackenbach JP, Steyerberg EW, Raat H, Verbrugh HA, Tiemeier HW, Hofman A, Birnie E, Looman CW, Jaddoe VW, Steegers EA. Individual accumulation of heterogeneous risks explains perinatal inequalities within deprived neighbourhoods. Eur J Epidemiol. 2011;26(2):165-80.
- 10. Poeran J, Borsboom GJ, de Graaf JP, Birnie E, Steegers EA, Bonsel GJ. Population Attributable Risks of Patient, Child and Organizational Risk Factors for Perinatal Mortality in Hospital Births. Matern Child Health J. 2014; in press
- 11. Atkin WS, Edwards R, Kralj-Hans I, et al. Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial. *Lancet.* 2010;375(9726):1624-1633.
- 12. Segnan N, Armaroli P, Bonelli L, et al. Once-only sigmoidoscopy in colorectal cancer screening: follow-up findings of the Italian Randomized Controlled Trial-SCORE. *Journal of the National Cancer Institute*. 2011;103(17):1310-1322.
- 13. Schoen RE, Pinsky PF, Weissfeld JL, et al. Colorectal-cancer incidence and mortality with screening flexible sigmoidoscopy. *The New England journal of medicine*. 2012;366(25):2345-2357.
- 14. Holme O, Loberg M, Kalager M, et al. Effect of flexible sigmoidoscopy screening on colorectal cancer incidence and mortality: a randomized clinical trial. *Jama*. 2014;312(6):606-615.
- 15. Quintero E, Carrillo M, Gimeno-Garcia AZ, et al. Equivalency of Fecal Immunochemical Tests and Colonoscopy in Familial Colorectal Cancer Screening. *Gastroenterology*. 2014.
- 16. Imperiale TF, Ransohoff DF, Itzkowitz SH. Multitarget stool DNA testing for colorectal-cancer screening. *The New England journal of medicine*. 2014;371(2):187-188.
- 17. Heer J, Bostock M, Ogievetsky V. A tour through the visualization zoo. Communications of the ACM. 2010 Jun.;53(6).
- 18. Zhang Q, Segall R, Cao M (eds). Visual analytics and interactive technologies: data, text, and web mining applications. IGI Global, 2010.
- 19. Moore JH, Lari RC, Hill D, Hibberd PL, Madan JC. Human microbiome visualization using 3D technology. *Pacific Symposium on Biocomputing. Pacific Symposium on Biocomputing*. 2011:154-164.
- 20. Lv Z, Tek A, Da Silva F, Empereur-mot C, Chavent M, Baaden M. Game on, science how video game technology may help biologists tackle visualization challenges. PLoS One. 2013;8(3):e57990.