

Institution: University of Plymouth		
Unit of Assessment: UoA10		
Title of case study: Improved health research and practice through advancing statistical methods and applications		
Period when the underpinning research was undertaken: 2012 - present		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Dr Yinghui Wei	Associate Professor of Statistics	2013 – present
Dr Malgorzata Wojtys	Lecturer in Statistics	2013 – present
Period when the claimed impact occurred: 2015 – 31.12.20		
Is this case study continued from a case study submitted in 2014? N		
<p>1. Summary of the impact (indicative maximum 100 words)</p> <p>Dr Yinghui Wei's research on novel medical statistics has:</p> <ol style="list-style-type: none"> 1) Provided information through a Cochrane review on the significance of cutting portion size which informed Public Health England's sugar reduction report. Moreover, it raised public awareness of the importance of portion size and led to it becoming a key principle of weight management. Internationally, it informed the World Health Organization and Australia's Victorian Health Promotion Agency. 2) Created a statistical package which significantly reduces the time, resources required, and costs of individual participant survival data collection. 3) Produced a statistical analysis which has enabled kidney transplant doctors to understand the change of survival benefit of transplants over time, assisted with decision-making about treatment options in their clinical practice and enabled doctors to communicate better with their patients. 		
<p>2. Underpinning research (indicative maximum 500 words)</p> <p>Research led by Dr Yinghui Wei at the University of Plymouth (UoP) in collaboration with colleagues from University Hospitals Plymouth NHS Trust, UCL, and Universities of Cambridge, Nottingham and Bristol, has focused on the following themes.</p> <p>a) Statistical analysis in evidence synthesis</p> <p>The Cochrane sizing review [3.1] suggested that cutting portion, packaging and tableware size presented a potential path to tackle obesity, which impacts a quarter of British adults, costing lives and quality of life. Wei co-led the statistical analysis in this review to evaluate the effect of portion, package, individual unit and tableware size on changing the consumption of food, alcohol and tobacco [3.1]. She conducted a meta-analysis of 86 independent comparisons from 58 studies (6,603 participants), which concluded a statistically significant effect of portion, package, individual unit or table size on food consumption (standardised mean difference, 0.38, 95% CI: 0.29 to 0.46), providing evidence that exposure to larger sizes increases quantities of food consumption, regardless of factors such as gender and BMI.</p>		

Other statistical analysis research included a network meta-analysis in [3.2], which allowed the simultaneous evaluation of eight different treatment options for patients with localised prostate cancer, by combining results from 21 randomised trials that included 3,450 men. Wei and collaborators also implemented stochastic transmission models and combined the results across multiple wards in intensive care units in an US hospital to evaluate the control measures consisting of gown and glove as well as isolation room management in minimising the spread of antimicrobial-resistant pathogens [3.3].

b) Regenerating individual level time-to-event data for health technology assessments

Meta-analysis plays a central role in health technology assessments. Individual participant data (IPD) meta-analysis is a gold standard of systematic reviews. However, collecting IPD from multiple studies is time consuming, and often takes months to years, with inevitable funding implications.

Wei led the development of the statistical package *ipdfc* in Stata [3.4], which enables the accurate regeneration of the individual participant time-to-event data by using the information extracted from published survival or cumulative incidence curves. The regenerated data can be used to estimate hazard ratios as well as conduct secondary analyses, and hence enable the best use of the available evidence for health technology assessments.

c) Survival analysis in kidney transplant

Since 2015, Wei conducted statistical analysis for the annual reports of the South West Transplant Centre (SWTC). Wei estimated the difference in restricted mean survival time (RMST) [3.5] between living and deceased donor recipient groups for kidney graft survival and overall patient survival, respectively. The difference in RMST between treatment groups gives an interpretation of the gain/loss in life expectancy in any defined unit measurement of time. Her team extended copula models [3.6] to survival analysis to estimate the correlation coefficient between kidney graft failure and death, which gives an insight into the strength and direction of the association. They also applied these novel methods to the transplant national database from NHS Blood and Transplant (NHSBT). Since data from multiple transplant units are available, the results of the difference in RMST are combined using statistical methods described in [3.5]. This ongoing collaboration with the SWTC has resulted in them providing funding for a PhD project to develop risk prediction models to assist clinical decision making in kidney transplant.

3. References to the research (indicative maximum of six references)

- 3.1 Hollands G., Shemilt I., Marteau T.M., Jebb S.A., Lewis H.B., **Wei Y.**, Higgins J.P. and Ogilvie D. (2015) Portion, package or tableware size for changing consumption of food, alcohol and tobacco: a Cochrane intervention review (full review). *Cochrane Database of Systematic Reviews*, Issue 9.
- 3.2 Xiong T., Turner R.M., **Wei Y.**, Neal D.E., Lyratzopoulos Y. and Higgins J.P. (2014) Comparative efficacy and safety of treatments for localized prostate cancer: an application of network meta-analysis. *BMJ open*, 4, issue 5.
- 3.3 **Wei Y.**, Kypriaos T., O'Neill P.D., Huang S.S., Rifas-Shiman, S.L. and Cooper B.S. (2018) Evaluating hospital infection control measures for antimicrobial-resistant pathogens using stochastic transmission models: application to vancomycin-resistant *enterococci* in intensive care units. *Statistical Methods in Medical Research*, 27(1): 269-285.
- 3.4 **Wei Y.**, Royston P. (2017) Reconstructing individual-level time-to-event data using published Kaplan-Meier curves. *The Stata Journal*, 17(4), 786-802.
- 3.5 **Wei Y.**, Royston P., Tierney J.F. and Parmar M.K. (2015) Meta-analysis of time-to-event outcomes from randomized clinical trials using restricted mean survival time: application to individual participant data. *Statistics in Medicine*, 34(21), 2881-2898.
- 3.6 **Wojtyś M.**, Marra G. and Radice R. (2016) Copula regression spline sample selection models: the R package SemiParSampleSel. *Journal of Statistical Software*, 71(6), 1-66.

Research Grants

We have secured research grants totalling over £332K as detailed below, to establish our medical statistics research.

(2020 – 2024) **Wei Y.**, PI, NHS and EPSRC, “Using big data to develop and validate clinical prediction models for survival outcomes in kidney transplant”, £77,173.

(2019 – 18 months) **Wei Y.**, Co-I, GSK, “An assessment of the sensitivity to change of a scale to measure quality of life in patients with severe asthma”, PI: Jones R. at the University of Plymouth, £55,754.

(2019 – 12 months) **Wei Y.**, Co-I, GSK, “Further validation of a scale to measure quality of life in patients with severe asthma”, PI: Jones R. at the University of Plymouth, £44,503.

(2016 – 2018) **Wei Y.**, Co-I, NIHR Research for Patient Benefit “A systematic review of physical activity for alcohol and substance use disorders: evidence synthesis with stakeholder engagement to formulate practical recommendations”, PI: Thompson T. at the University of Plymouth, £154,528.

4. Details of the impact (indicative maximum 750 words)

a) Government policy change in food and drink sectors

Obesity has become one of the major challenges of our time. It is a complex condition, with significant contributions from genetic factors, physiological factors, environmental factors, and social and psychological factors that influence diet and activity. About two thirds of UK adults are now overweight and nearly one third are obese. Obesity alone accounts for at least 10% of NHS spend, and this is rising. Therefore, the prevention and treatment of obesity has become a national priority. In the UK, NICE guidance “*Obesity: Identification assessment, management*” identified the broad principles of dietary (and other) treatments, including the aim of achieving an energy deficit while maintaining a healthy and balanced diet. However, the guidance did not provide detailed guidance on how this can be achieved.

Wei and colleagues Cochrane sizing review and meta-analysis rectified this problem by providing important evidence demonstrating that reducing the size of food portions and tableware can be used as a strategy for weight loss. The review was cited in Public Health England’s (PHE) October 2015 publication *Sugar reduction: The evidence for action* report [5.1], which had been commissioned by the Department of Health to feed into the Government’s childhood obesity strategy. PHE’s report highlighted Wei’s review to argue for the benefits of reducing portion sizes. This was then used to create a programme of gradual sugar reduction in food and drink combined with the reduction in portion size and led to the development of various tools such as the Eatwell Guide, that assist patients in achieving weight loss. *‘[Wei’s] evidence-based strategy has become a key principle of weight management and is now firmly embedded within weight management programmes such as ours, and elsewhere in the UK and worldwide’*. Professor Jonathan Pinkney, Consultant Physician, Plymouth and West Devon Weight Management Service, Livewell South West [5.2].

Wei’s research raised public awareness on portion size and regularly receives media attention in news and television programmes 5.3. This has resulted in the concept of portion control being universally recognised as a fundamental requirement for the prevention of weight gain and its associated health comorbidities, and for achieving weight loss. This is evidenced by a wide range of websites, both nationally and internationally, who use this strategy (e.g., British Heart Foundation, the British Nutrition Foundation and the British Dietetic Association) [5.2].

Internationally, the World Health Organization e-library of Evidence for Nutrition Actions quoted Wei’s review to argue for “*limiting portion sizes to reduce the risk of childhood overweight and obesity*” [5.4]. Moreover, the findings of the review were shared with Australia’s Victorian Health Promotion Agency (VicHealth) [5.5] and used in their subsequent citizen jury which resulted in a recommendation that beverage sizes should be regulated and that a maximum size of soft drinks and other calorie-dense beverages that can be sold through restaurants and retail outlets should be imposed.

b) Saving time and costs in data collection and analysis

Individual participant data (IPD) meta-analysis is a quantitative method in evidence synthesis using the original research data sought directly from the researchers responsible for each study. This collection of individual raw data is time intensive (often taking months to years), usually requires dedicated staff with a variety of skills and it costs more than a conventional meta-analysis of published or other summary data. Wei's innovative statistical package *ipdfc* [3.4] used published curves to generate individual participant data which reduced the time of data collection and at no cost. As of November 2020, the package has been downloaded more than 153 times from the *Stata Journal* site [5.6], with users in the UK, USA, China, Spain, France, Netherlands, India, Singapore and Switzerland.

A bioinformatician from Switzerland confirmed that Wei's package provides a significant benefit in its simplicity in implementation and accuracy on extrapolating individual-level data. This statistical package can potentially help clinicians with decision making for health technology assessments by estimating statistical robustness of trials, evaluating the benefit of treatments, and enhancing communication with patients [5.7]. [text removed for publication], says. *'I would like to emphasize that 'ipdfc' is exceptionally accurate in our experience.... In summary, using your statistical package has provided me with significant benefits. It has enabled [us] to reduce the time of data collection from months and years to a few minutes and at zero financial cost.'* [5.7].

A Spanish hospital confirmed that Wei's package has enabled their team to reconstruct a database for five studies of 4,686 patients, producing evidence of the long-term survival benefit of a mechanical valve compared to biological aortic valve replacement in patients with heart diseases. Their previous methodology frequently produced incorrect conclusions and Wei's package enabled them to strengthen their methodology. The calculation has allowed them to understand which group has a lower risk of death. *'The package has contributed to producing reliable information which we are confident in, and I found it is more accurate than the other packages for regenerating the original survival data. Your work has been very beneficial... allowing us to increase our understanding of the research questions. The package has informed and benefitted our research practice enabling us to perform alternative statistical analyses'*. [text removed for publication] [5.8].

c) Enhancing communication of survival outcomes in kidney transplant

In the UK, about three million lives are affected by kidney diseases. Every year, about five thousand patients are active on the kidney transplant waiting list and more than 3,000 patients receive kidney transplants in the UK. Every donor kidney is different and when it is offered to a waitlisted candidate, the clinical team responsible for the care of the potential recipient must make the decision to accept or decline the offer within a short period of time and based upon complex and variable information about the donor, the recipient and the process of transplantation. Wei's research in kidney transplant survival analysis provided enhanced information, supporting treatment planning and enabling doctors' communication with patients in a more intuitive way. *"Thank you for your contributions to the statistical analysis for the kidney transplant data... 2015, 2016, 2017, 2018. This has helped us for the audit of survival outcomes of patients following kidney transplant... [this] is of interest to clinicians and will provide a new piece of medical information which will be helpful in communications with patients"*. [text removed for publication] [5.9].

In 2019, Wei and her team presented their RMST application at the SWTC annual transplant day. This day is approved as Continuing Professional Development by the Royal College of Physicians. The event was attended by 57 participants (22 doctors, 15 nurses, 14 statisticians, 4 biomedical scientists, one pharmacist and one lay person). A UoP commissioned independent evaluation of the event confirmed that doctors find Wei's application valuable. One doctor said, *"As a clinician, I feel that RMST is very intuitive and easier to explain/more relevant to patients/practice"*. Seventy-one percent of doctors said that the use of RMST had enabled them to explain years/months gain/loss in life expectancy since transplant and 67% found RMST easier to understand than the hazard ratio. Visualisation of the difference in RMST helped

doctors to understand the change of survival benefit of transplants over time (71%), and 42% of doctors reported the RMST assisted with decision-making about treatment options in their clinical practice. [text removed for publication] said “*Your presentation... received extremely positive feedback. Of the participants that responded, 92% said that they found it useful.*” [5.9].

5. Sources to corroborate the impact (indicative maximum of 10 references)

- 5.1 Public Health England, “[Sugar reduction: the evidence for action report](#)”, 2015.
- 5.2 Testimonial Professor Jonathan Pinkney BSc MB BS, MD FRCP Consultant Physician, Plymouth and West Devon Weight Management Service, Livewell South West, Plymouth.
- 5.3 NHS Choices, [Decreasing portion sizes could cut obesity levels](#), 2015.
- 5.4 WHO e-Library of Evidence for Nutrition Actions, [Limiting portion sizes to reduce the risk of childhood overweight and obesity](#), 2019.
- 5.5 The Cochrane Review on portion sizes - from publication to informing policy <https://www.cochrane.org/news/cochrane-review-portion-sizes-publication-informing-policy>
- 5.6 Email from the *Stata Journal* Production Manager, 2020.
- 5.7 Testimonial [text removed for publication].
- 5.8 Testimonial [text removed for publication] 2019.
- 5.9 Testimonial [text removed for publication] 2019.
- 5.10 Testimonial [text removed for publication], 2019.