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ABSTRACT

Knowledge trajectory in science represents what research has been conducted. This article examines whether maintaining or changing knowledge trajectory improves subsequent research performance. The focus is on how knowledge trajectory changes affect academic performance when scientists choose research subject that deviates from previous research. Publicly funded research projects of induced pluripotent stem cell (iPSC) in Japan were analyzed. Findings show that projects led by scientists that have stem cell research history have published more articles in international peer-reviewed journal than those led by scientists that are otherwise. Additionally, the impact of leaders' stem cell research history on project performance intensified after a Japanese scientist won the Nobel Prize in Physiology or Medicine in 2012 for discovering iPSC. These findings suggest that a targeted policy could affect academic performance if it decides scientists' research subjects.

KEYWORDS: Knowledge trajectory, Public research, Stem cells

1. INTRODUCTION

Past knowledge is a foundation for future research and shapes scientific knowledge trajectory (Foster, Rzhetsky, and Evans, 2015; Nelson, 1959; Uzzi et al., 2013). Prior research has investigated the factors that affect knowledge accumulation process to

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improve academic performance. For example, Furman and Stern (2011) illustrate the effectiveness of economic institutions that promote knowledge diffusion among researchers. Azoulay, Zivin, and Manso (2011) find that tolerance for changing research subjects and project evaluation timelines influence research performance. They compare the performance of investigators funded by the Howard Hughes Medical Institute (HHMI) with those funded by the National Institutes of Health (NIH). HHMI allows scientists to change research subjects and evaluates their performance from a long-term perspective, whereas NIH does not allow in research subject changes and adopts a renewal system based on a short-term evaluation. The result shows that HHMI investigators broaden their research focus after their appointment. Additionally, Sampat (2012) refers that public funding with a definite target induces research to a specific subject. Li, Azoulay, and Sampat (2017) find that NIH-funded projects increase relevant patents in the industry. Their findings indicate that targeted public funding affects scientists' research subjects choices and has a ripple effect on relevant industry growth. By contrast, the impacts of changes in scientists' subject choices on future research remain unexplained.

Previous research has consistently recognized the positive impact of public investment in Research and Development on academic performance (Arrow, 1962; Dasgupta, 1994; Davidson and Potts, 2016). Particularly, public funding plays significant roles in giving scientists incentives for novel sciences. For example, Packalen and Bhattacharya (2020) find that NIH tends to allocate more budget to novel sciences than to conservative subjects. Corredoira, Goldfarb, and Shi (2018) find that federal government funding supports projects that significant impact newly developing areas. By contrast, recent research has referred that targeted public funding directs scientists to choose specific research. Jung and Lee (2014) describe that mission-oriented policy promotes scientists' myopic choices. They evaluate the effect of a U.S. government science program launched in 2001, namely, the National Nanotechnology Initiative, on university research. Their findings show that as industry knowledge inflow increases, research subjects become narrower and less diverse in universities. This finding is due to the industry's promotion of focused research and technology commercialization. Additionally, Blume-Kohout (2012) finds that targeted funding from NIH for specific diseases increases the number of relevant drugs for such diseases. This article adds to the evidence of how targeted policy-driven research incentives affect scientists' research subject choices and their academic performance.

This article reveals the impact of scientists' research subject choices that are driven by targeted policy on subsequent research. Targeted policy gives scientists

incentives to choose specific research subjects. When grant incentives motivate them to choose research subjects that deviate from their research history, the choices could have positive and negative effect on their academic performance. A positive scenario pertains to research that would not be bound by past studies. Scientists are unlikely to change their research subjects to maintain their knowledge trajectory for stable academic performance (Foster, Rzhetsky, and Evans, 2015). Foster, Rzhetsky, and Evans (2015) suggest that policy would significantly trigger them to choose non-traditional research. A negative scenario occurs when a vulnerable research plan with insufficient preparation degrades researchers' academic performance. This article articulates the interventions of targeted policy that change scientists' knowledge trajectories and investigates the impact of their research subject changes on academic performance.

Stem cell research in Japan is appropriate for this analysis because political support is skewed toward research of induced pluripotent stem cell (iPSC). The rationale of skewness is that iPSC could be induced to any human body cell given its pluripotency. iPSC couldf overcome the challenges of existing treatments of various diseases. The skewed political support would be partly attributable to the discovery of iPSC by a Japanese scientist who won the Nobel Prize in Physiology or Medicine 2012. The skewness provides scientists incentives to choose iPSC as a research subject. Therefore, the context of publicly funded stem cell research fits the purpose of this article.

This analysis examines how targeted policy for iPSC and knowledge trajectory changes caused by the targeted policy influence scientists' research subject choices and their academic performance, respectively. Certain scientists with research subjects about stem cells are likely to be interested in iPSC. Nevertheless, other scientists whose research interests have been distant from stem cells may also choose iPSC research because of the perception that political support for this research increases its amount of grant. The issue is whether these scientists could achieve the expected performance given their lack of knowledge and research history of stem cells. Thus, this article analyzes how scientists' stem cell research history affects their academic performance in iPSC research. Results show that projects led by scientists with no experiences of publicly funded stem cell research projects publish less articles in international peer-reviewed journals than those led by scientists that are otherwise. Additionally, the data demonstrate that publicly funded iPSC research has increased, particularly those led by scientists with no publicly funded stem cell research. This finding suggests that when support for health mission is limited to iPSC, the narrow target excluding other stem cell options would account for the vulnerability of cumulative knowledge in future stem cell research.

The remainder of this article is structured as follows. Section two explains the

contribution of this article and discusses the factors that determine the type of knowledge accumulated in scientific research. Section three describes the hypotheses, and Sections four and five present the sample data and research method, respectively. Then, Section six refers to the methodology, and Section seven presents the results. Lastly, Section eight discusses the roles of prior knowledge in scientific research and suggests the effectiveness of scientists' discretion to choose research subject and concludes the artilce.

2. FACTORS AFFECTING SCIENTISTS' RESEARCH SUBJECT CHOICES

Scientific knowledge trajectory depends on scientists' history of research subject choices. Prior research has investigated the factors that affect their choices and found that knowledge continuity in research projects depends on various factors. These factors include public support for existing technologies (Finkelstein, 2004), the disease prevalence that directs medical research (Battacharaya and Packalen, 2011), state funding for stem cell research (Alberta et al., 2012), political restrictions of research funding for specific stem cell research (Furman, Murray, and Stern, 2012), death of star scientists (Azoulay, Fons-Rosen, and Zivin, 2019), and the advent of equipment that automates research tasks (Furman and Teodoridis, 2020). Targeted public funding is one of the factors on which prior research has focused because it affects how scientists advance biomedical innovation (Alberta et al., 2012; Furman, Murray, and Stern, 2012; Packalen and Bhattacharya, 2020; Sampat, 2012).

Knowledge continuity has mixed impacts on project performance, though previous research shows that existing knowledge significantly forms the foundations of subsequent projects (Foster, Rzhetsky, and Evans, 2015; Nelson, 1959; Uzzi et al., 2013). Positive impacts refer to radical innovation that depends on an extension of existing knowledge. Organizations that have relevant technical knowledge within their boundaries successfully achieve innovation (Cohen and Levinthal, 1990; Roy and Salker, 2016). Uzzi et al. (2013) find that high-impact research has been published through exceptional combinations of conventional knowledge. By contrast, negative impacts refer to existing knowledge that limits the scope of search, though it improves search efficiency (March, 1991). March (1991) suggests that an organizational mechanism is crucial to promoting distant search for radical innovation. Stuart and Podolny (1996) find that strategic alliances provide firms with opportunities to break the constraints of local search.

Whether project leader-level knowledge continuity is significant for research performance is noteworthy because targeted science policy should be designed to induce scientists that have optimal attributes to engage in specific research. This article assumes that targeted political support could promote research projects that are distant from the

past. It addresses the case where a narrow focus of a policy target gives scientists incentives to pursue iPSC research. Conclusions would suggest the optimal balance of political support regarding the range of the target.

3. HYPOTHESES

To investigate how knowledge trajectory influences subsequent scientific research, this article focuses on publicly funded stem cell research in Japan. This provides optimal research settings. The targeted policy for stem cell research has been skewed toward iPSC in Japan. iPSC as a research subject attracts scientists' interests because it facilitates public research grant acquisition. However, whether scientists that are incentivized by the targeted policy to start iPSC research could achieve the expected performance remains unclear. These scientists may deteriorate project performance, except when they have prerequisite stem cell knowledge. This article focuses on scientists' stem cell research history and explores its contribution to iPSC research project performance.

Stem cells have several types. In constructing the variables about research history, this article focuses on the following five types of major stem cells. First, iPSC is a pluripotent stem cell, and it can be differentiated into cells that comprise multiple human body tissues. Embryonic stem cells (ESC) are categorized under this type of stem cells and an alternative to iPSC for scientists. However, using ESC for research causes ethical issues as it is made from fertilized eggs. Thus, iPSC is an attractive tool for scientists because it does not such an issue. The production processes of iPSC and ESC have artificial steps. Second, mesenchymal stem cell (MSC) also exhibits pluripotency, and it can be differentiated into several cells and tissues. However, its original presence in the human body differentiates it from iPSC and ESC. Finally, somatic stem cells (SSC) can be differentiated into specific human body tissues, whereas cancer stem cells (CSC) are relevant to cancer growth and can be self-renewal.

A surrogate variable of a knowledge trajectory relevant to scientists is their stem cell research history before iPSC research projects. The maintenance of a trajectory is defined as the distance from existing knowledge space, following Furman and Teodoridis (2020). Stem cell research history shortens the distance between past knowledge space and iPSC research. Scientists could find satisfactory paths to the project's goal from alternatives easily and cost-efficiently with relevant knowledge (Nelson, 1959). (Nelson, 1959). Thus, researchers with relevant knowledge may achieve higher performance than otherwise. Therefore, the analysis focus on whether scientists that starts iPSC research despite their lack of stem cell research history could achieve high iPSC

research performance.

Hypothesis 1 (H1) holds that scientists with stem cell research experience could achieve higher academic performance than those that are otherwise because they could recognize iPSC superiority regardless of targeted policy. Rich stem cell knowledge contributes to improving academic performance. Thus, experienced scientists would publish more articles than those who are incentivized by targeted policy to start iPSC research without stem cell research history. H1 examines whether project leader-level stem cell research history affects project-level academic performance. Therefore, H1 holds that projects led by scientists with stem cell research history achieve higher iPSC research performance than those led by scientists with no relevant knowledge.

H1. Projects led by scientists with stem cell research history achieve higher iPSC research performance than those led by scientists with no relevant knowledge.

Hypotheses 2a–c (H2a–c) focus on scientists' research history of pluripotent stem cells and examine whether projects led by scientists that have experiences of working with ESC, MSC, and iPSC achieve higher performance than those led by scientists that do not. iPSC must have attracted alternative to the interest of scientists with ESC research history given its lack of ethical issues. H2a–b hold that projects led by scientists that have ESC and MSC research history achieve higher iPSC research performance than those led by scientists that do not. By contrast, the number of scientists that have iPSC research history increases after its discovery in 2006 (Takahashi and Yamanaka, 2006). Therefore, H2c holds that projects led by scientists with iPSC research history achieve higher research performance than those led by scientists that are otherwise.

H2a. Projects led by scientists with ESC research history achieve higher iPSC research performance than those led by scientists that are otherwise.
H2b. Projects led by scientists with MSC research history achieve higher iPSC research performance than those led by scientists that are otherwise.
H2b. Projects led by scientists with iPSC research history achieve higher iPSC research performance than those led by scientists that are otherwise.

Hypothesis 3 (H3) focuses on SSC to examine the impact of leader scientists' stem cell research history on the academic performance of iPSC research projects.

Scientists aim to regenerate tissues damaged by injuries and disease through iPSC-derived SSC. Their rich SSC knowledge would increase the academic performance of iPSC research projects. Therefore, H3 holds that projects led by scientists with SSC research history achieve higher iPSC research performance than those led by scientists that are otherwise.

H3. Projects led by scientists with SSC research history achieve higher iPSC research performance than those led by scientists that are otherwise.

H4 focuses on CSC to examine the impact of leader scientists' stem cell research history on the academic performance of iPSC research projects. CSC differs from other stem cells in that it is the target to eradicate. Scientists develop cancer eradication methods through iPSC-derived CSC. Their abundant CSC knowledge increases iPSC research performance. Therefore, H4 holds that projects led by scientists with CSC research history achieve higher iPSC research performance than those led by scientists that are otherwise.

H4. Projects led by scientists with CSC research history achieve higher iPSC research academic performance than those led by scientists that are otherwise.

Hypothesis 5 (H5) examines how the 2012 Nobel Prize mediates the relationship between project leaders' stem cell research history and the academic performance of iPSC research projects. High evaluations for iPSC could influence perceptions of relevant research. The 2012 Nobel Prize would have attracted scientists' research interest toward iPSC and could affect reviewers' decisions in screening the proposals for public grants and their positive perception of iPSC research. For example, Azoulay, Stuart, and Wang (2014) find that scientists that have become HHMI investigators increase citations in their articles that were published before their appointment. These circumstances would increase the number of publicly granted iPSC research projects. Thus, the proportion of projects led by scientists without stem cell research history would increase. Accordingly, H5 holds that the impact of a leader's stem cell research history on iPSC research project academic performance intensifies after the 2012 Nobel Prize than before it was awarded

to the Japanese scientist for discovering iPSC.

H5. The impact of a leader's stem cell research history on the academic performance of iPSC research projects intensifies after the 2012 Nobel Prize than before it was awarded to the Japanese scientist for discovering iPSC.

4. DATA AND VARIABLES

The analysis of this article focuses on publicly funded research projects to investigate the impact of knowledge continuity on academic performance. Certain research has used patents to quantify and visualize a knowledge trajectory. Patent citations quantify knowledge flow and examine the impact of accumulated knowledge on economic growth, research productivity, and business strategy (Jaffe and Trajtenberg, 2002; Li, Azoulay, and Sampat, 2017; Roach and Cohen, 2013; Roberts et al., 2014; Stuart and Podolny, 1996). In recent years, Azoulay et al. (2019) demonstrate that a $10 million increase in NIH funding generates additional 2.7 relevant patents in the private sector. Their results show that NIH's public funding allocation affects scientists' research subject choices and changes a knowledge trajectory. Additionally, Sampat and Williams (2019) analyze the selection mechanism of innovation for patenting and find that patented genes are more significant than non-patented ones. Their conclusion suggests that patented knowledge is biased in organizational decision making. By contrast, iPSC research is still nascent in the stem cell research field, and patents would not reflect the latest iPSC research trend. Therefore, scientific paper analyses could appropriately articulate scientists' behaviors for this article.

The sample data of this study comprise publicly funded iPSC research projects in Japan. To construct the dataset, sample data are selected up from research projects that receive public funding from Grant-in-Aid for Scientific Research (KAKEN). The sample includes projects whose titles contain "iPS" or "induced pluripotent stem cells" and that started in the academic year 2009–*Year* 2017 and finished by the academic year 2018. Japan's academic year is from April to March of the following year. Incomplete projects by the end of the academic year 2018 are removed from the sample because they create poor performance bias. Publishing articles in peer-reviewed journals takes some time. Thus, including the entire project duration is significant in determining the number of published articles. The initial year of the sample period is 2009 during which the number of publicly funded iPSC research projects began to grow after the discovery of iPSC in

2006 (Takahashi and Yamanaka, 2006). The last year of the sample period is 2017, the year when the number of published papers could have been counted for two years by the end of the project at the time of data collection in December 2019. The sample data include 722 scientists and 936 projects.

Scientific research performance is measured by the number of articles that have been published from projects granted by the KAKEN funding. Project leaders are obliged to report the performance of KAKEN-funded research projects. Publications in the report include conference proceedings, articles in peer-reviewed journal, handbook chapters, and essays in university bulletin that is published from institutions to which project members belong and whose editorial board members are usually only researchers of publishers. The dependent variable is *Number of articles*, which includes articles published in international peer-reviewed journals only. To construct the sample data, the author screened manually published articles in international peer-reviewed journals from the performance list of the respective report.

The independent variable, *Stem cell*, for H1 determines whether project leaders have stem cell research history. *Stem cell* is binary data that equals 1 if project leaders had conducted KAKEN projects whose titles include "ESC," "MSC," "iPSC," "SSC," "CSC," or "pluripotent stem cells" and 0 otherwise.

The independent variables, *ESC*, *MSC*, *iPSC*, *SSC*, and *CSC*, for H2–4 determine whether project leaders have respective stem cell research history. These variables are binary data that equal 1 if project leaders had conducted KAKEN projects whose title had the respective stem cell term and 0 otherwise. For example, *ESC* equals 1 if they had conducted publicly funded projects whose title included ESC and 0 otherwise. Projects whose titles include multiple stem cells are counted in respective stem cell. For example, *ESC* and *MSC* equal 1 if the project leader had conducted a project whose title included ESC and MSC. The sample data comprise 348 and 588 projects led by scientists with and without stem cell research history, respectively.

The control variables are *Amount of grant (logged)*, *Specific grant for young scientists*, *Nobel Prize*, and *Year 2009–Year 2016*. *Amount of grant (logged)* is the logged total amount of grant per project and controls whether abundant financial resources allow easier publication of articles. *Specific grant for young scientists* determines whether the grant is specific for young scientists and controls the period of project leaders' research history. Senior scientists are more likely to have stem cell research history than younger ones due to their longer careers. This specific grant is allocated to scientists under 40 years old at the start of the research project, and the sample contains 339 recipients of this grant. This control variable is used only to examine H1 because the number of recipients

per stem cell is small. *Specific grant for young scientists* is a dummy variable that equals 1 if a type of project grant is specific for young scientists and 0 otherwise. *Nobel Prize* determines whether projects started before 2012, the year when the Japanese scientist received the 2012 Nobel Prize for the discovery of iPSC. It controls whether the impact of scientists with stem cell research history on performance would intensify after the 2012 Nobel Prize. *Nobel Prize* is a dummy variable that equals 1 if a project starts after 2013 and 0 otherwise. *Year 2009–Year 2016* are dummy variables for the start year of respective projects and control the influence of stem cell research history that has intensified since the iPSC discovery. The later the projects start in the sample period, the stronger the impact of stem cell research history on performance is. *Year 2009–Year 2016* are binary data that equal 1 if a project started in its respective year and 0 otherwise. For example, *Year 2009* equals 1 if a project started in the academic year 2009 and 0 otherwise. *Year 2017*, which is the last year of the sample period, is not set as a dummy variable because it has less data than the other start years. The small number of *Year 2017* is due to unfinished projects in March 2019, which are excluded from the sample.

5. TREND OF iPSC RESEARCH PROJECTS

Graph 1 demonstrates the number of projects with "iPSC" in their titles by start year. It shows that the number of iPSC research projects significantly increased in 2012–2014. The decrease in 2017 is due to excluded incomplete projects by the end of the academic year 2018. One, two, and 97 projects started in 2015, 2016, and 2017, respectively, were incomplete by the end of the academic year 2018 and removed from the dataset. By contrast, the average number of articles published in international peer-reviewed journals per project and start year had decreased in 2012–2014. The recovery of average number is observed in 2015 due to a project that reported to publish 119 articles in international peer-reviewed journals. The average value is 5.12 in 2015, excluding this project, and the downward trend is continuous.

Graph 2 compares the average number of articles per project led by scientists with and without stem cell research history. Throughout the sample period, projects led by scientists with stem cell research history have published more articles than those led by scientists that are otherwise. The difference between the two groups is large in 2013 and 2014. Within two years after the 2012 Nobel Prize, the number of published articles has dropped significantly in projects led by scientists without stem cell research history. In 2015, the average value per project led by scientists without stem cell research history is approximately 4.19, excluding a project that had published 119 articles as mentioned in the previous paragraph. However, the difference between the two groups in 2015

becomes less than that in 2013 and 2014. The decrease in the average value in 2017 is due to the same reason as described in Graph 1.

Graph 3 demonstrates the proportion of projects led by scientists with respective stem cell research history by start year. This proportion is calculated by dividing the number of research projects led by scientists with respective stem cell research history by the total number of projects that start in each year. Although the proportion of projects led by scientists with iPSC research history has demonstrated an increasing trend during the sample period, those led by scientists with ESC and SSC research history have been in a decreasing trend.

The three graphs suggest that the impact of leader scientists' stem cell research history on project performance may be strongly observed within the next two years after the 2012 Nobel Prize. The total number of iPSC research projects increases, whereas the average number of published articles per project decreases. The trend of respective stem cells in Graph 3 shows that the proportion of projects led by scientists with research history of ESC, MSC, iPSC, and SSC has decreased in projects that started in 2013 during which the total number of projects has increased significantly.

<Graph 1. Number of projects and average number of articles per project and start year>

<Graph 2. Average number of articles per projects led by scientists with and without stem cell research history>

< Graph 3. Proportion of projects led by scientists with respective stem cell research history>

6. METHODOLOGY

The analysis is conducted at the project level to investigate the impact of project leaders' stem cell research history on the number of published articles in publicly funded iPSC research projects. The dependent variable is the number of articles for H1–5. Because it is a count data that is a non-negative integer and exhibits overdispersion whose variance and mean are 67.05 and 5.38, respectively, a negative binomial regression approach is appropriate (Cameron and Trivedi, 1998). The dataset comprises the number of articles from iPSC research projects, project leaders' stem cell research history, and four control variables.

H1 examines the influence of stem cell research history on academic performance. H2–4 examine the type of stem cells in project leaders' research history that influences the academic performance of iPSC research projects. H5 examines whether the impact of project leaders' stem cell research history on academic performance has changed around the 2012 Nobel Prize. The coefficients of independent variables are compared between the projects that started before and after 2013.

7. RESULTS

Tables 1–3 demonstrate the descriptive statistics of all variables, their correlations, and negative binominal regression results, respectively.

Models 1–2 examine the effect of *Stem cell* on *Number of articles* for H1. The two models have different control variables about grant type, before and after the 2012 Nobel Prize, and start year of the projects. *Specific grant for young scientists* and *Nobel Prize* are used for Model 1, and *Year 2009–Year 2016* are used for Model 2. *Specific grant for young scientists* is used only for Model 1, because the number of recipients of specific grant for young scientists per respective start year is small. In Model 1, the coefficient of stem cell research history is positive and statistically significant at the 5 percent level. Projects led by scientists with stem cell research history publish more articles than those led by scientists that are otherwise, thus supporting H1. The coefficient of *Amount of grant (logged)* is positive and statistically significant at the 1 percent level. The greater the grant amount is, the more articles are published per project. The coefficient of *Specific grant for young scientists* and *Nobel Prize* are negative and statistically significant at the 1 percent level. The younger the scientists are, the fewer articles are published per project. After the Japanese scientist won the 2012 Nobel Prize for the discovery of iPSC, the number of published articles per iPSC research project had decreased. Model 2 examines the effect of *Stem cell* on performance by controlling for *Year 2009–Year 2016*. The coefficients of *Stem cell* and *Year 2009–Year 2015* are positive and statistically significant at the 1 percent level. The coefficients of *Year 2016* are positive and statistically significant at the 5 percent level. The values of the coefficients of *Year 2013-2016* are smaller than those of *Year 2009–Year 2012*.

Models 3–4 examine the effect of *ESC* on *Number of articles* for H2a. Although H2a holds that project leaders' ESC research history affects the number of articles per project, Models 3–4 demonstrate that the coefficient of *ESC* is positive and statistically insignificant. Models 5–6 examine the effect of *MSC* on *Number of articles* for H2b. The coefficient of *MSC* is statistically significant at the 10 percent level. Project leaders' MSC research history affects the number of articles per project, thus supporting H2b. Models

7–8 examine the effect of *iPSC* on *Number of articles* for H2c. Project leaders' iPSC research history affects the number of articles per project, thus supporting H2c. The coefficient of *iPSC* is statistically significant at the 10 percent and 5 percent levels in Model 7 and 8, respectively. Models 9–10 examine the effect of *SSC* on *Number of articles* for H3. The coefficient of *SSC* is statistically significant at the 5 percent level in Models 9–10. Project leaders' SSC research history affects the number of articles per project, thus supporting H3. Models 11–12 examine the effect of *CSC* on *Number of articles* for H4. The coefficient of *CSC* is statistically significant at the 10 percent level in Models 11–12. Project leaders' CSC research history affects the number of articles per project, thus supporting H4.

In Models 3–12, *Amount of grant (logged)* and *Nobel Prize* are control variables for odd-numbered models, whereas *Amount of grant (logged)* and *Year 2009–Year 2016* are those for even-numbered models. The coefficients of *Amount of grant (logged)* are positive and statistically significant at the 1 percent level in Model 3–12. The coefficients of *Nobel Prize* are negative and statistically significant at the 1 percent level in the odd-numbered models. In the even-numbered models, the coefficients of *Year 2009–Year 2015* and *Year 2016* are positive and statistically significant at the 1 percent and 5 percent levels, respectively.

Table 4 demonstrates the results of investigating the impact of respective stem cell research history on the number of articles around the 2012 Nobel Prize for H5. The independent variables in Models 13–24 are *Stem cell*, *ESC*, *MSC*, *iPSC*, *SSC*, *CSC*, and *Amount of grant (logged)*. The coefficients of respective stem cell except *CSC* are larger after than before the 2012 Nobel Prize, thus supporting H5. *Stem cell*, *MSC*, and *iPSC* and *SSC* after the 2012 Nobel Prize are statically significant at the 1 percent, 5percent, and 10 percent levels, respectively. *CSC* before the 2012 Nobel Prize and *Amount of grant (logged)* in all models are also statically significant at the 10 percent and 1 percent levels, respectively. The statistically significant coefficients of independent variables after the 2012 Nobel Prize are larger in the order of *MSC*, *Stem cell*, *SSC*, and *iPSC*.

<Table 1. Descriptive statistics>

<Table 2. Correlations>

<Table 3. Results of negative binomial regression>

<Table 4. Comparison of the impact of stem cell research history before and after the 2012 Nobel Prize>

8. DISCUSSION AND CONCLUSIONS

This article concludes that project leaders with stem cell research history positively affect the academic performance of iPSC research. This effect intensified after the 2012 Nobel Prize. Since 2013, the proportion of projects led by scientists with iPSC research history has demonstrated the increasing trend, and the proportion of projects led by scientists with SSC research history has demonstrated a decreasing trend. Although iPSC research history is positively associated with research performance, its coefficients are less than those of MSC, SSC, and CSC research history. Additionally, the average number of published articles per iPSC research project had decreased after the 2012 Nobel Prize. Therefore, projects led by scientists with insufficient stem cell research background before the start of iPSC research may have poor performance.

The analysis examines how scientists' stem cell research history affects project performance. Results partly support five hypotheses. Although project leaders' stem cell research history affects the number of articles in projects, the effect varies depending on the type of stem cells in research history and timing of the start of projects. The impact of scientists' iPSC research history is not as strong as that of MSC and SSC research history. The coefficient of iPSC in Model 22 is smaller than those of MSC and SSC in Models 18 and 22, respectively. ESC research history does not affect the performance of subsequent iPSC research projects.

The magnitude of the impact of research history changes around the 2012 Nobel Prize. H5 results demonstrate that the research history of MSC, SSC, and iPSC is statistically significant only after the 2012 Nobel Prize. A comparison of the impact of stem cell research history reveals that the case where project leaders have MSC research history has the largest coefficient after the 2012 Nobel Prize. Therefore, the decreasing proportion of projects led by scientists with MSC and SSC research history would partly explain the decline of the average number of articles per project in 2013–2014. Additionally, the increasing number of projects led by scientists with iPSC research history would not significantly offset the poor performance of projects led by scientists with no stem cell research history.

The hypothesis that scientists' ESC research history affects the number of articles per project is not supported, which might be due to the legal limit of ESC use in Japan. While the number of ESC projects in research history is modest, ESC research needs procedures for obtaining research permission from an ethical viewpoint. This laborious process might have hindered its further development. Additionally, H5 results demonstrate that project leaders' CSC research history contributes only to performance before the 2012 Nobel Prize. This finding may be explained by approaches other than CSC that may have appeared in research on cancer treatment using iPSC. These two unproven hypotheses would need more in-depth investigation based on a field research.

Targeted public funding could change the scientific knowledge trajectory, the impact of which would not be limited to scientific research. An increasing number of iPSC research projects caused by targeted public funding were further stimulated by the 2012 Nobel Prize. This event has a ripple effect on business development in surrounding areas, because private innovation is often rooted in publicly funded research (Azoulay et al., 2019). Public funding faces the tradeoff between short-term political agenda and long-term scientific progress. Packalen and Bhattacharya (2020) suggest that NIH should pursue both and that potential fields should be provided with ample funding to promote rapidly advancing fields. Accordingly, a policy focus on stem cell research would be appropriate. By contrast, Mazzucato and Semieniuk (2017) argue that public research funding has an objective of shaping and creating markets. Policymakers that develop public support skewed toward iPSC in Japan should have aimed at creating a market for regenerative medicine, because it included the Ministry of Economy, Trade, and Industry. Pursuing this economic objective may exclude diverse inefficient choices and lead to the simple skew toward iPSC.

Challenges associated with targeted policy include whether choosing iPSC as a research subject would be the optimal solution for scientists. For example, in the case of using stem cells to treat cardiac diseases, the candidate options are ESC, MSC, iPSC, and cardiac stem cells (Segers and Lee, 2008; Garbern and Lee, 2013). In addition to stem cells, the efficacy of treatment using skeletal myoblasts has been clarified, and a consensus on the best option for transplantation has not been reached (Garbern and Lee, 2013). Without political solicitation, the choice of iPSC to treat cardiac disease is left to the scientists' discretion. Political support for iPSC may have deprived scientists in Japan of choosing their optimal research subjects. Nelson (1959) describes that setting loose goals of basic research is rational, which could adapt to great uncertainty involved. This phenomenon would expect more payoff than closely defined goals (Nelson, 1959). Additionally, Comroe and Dripps (1967) investigate the accumulating process of essential

clinical knowledge in the field of cardiovascular and pulmonary diseases. Their results demonstrate that 41 percent of essential knowledge that later contributed to clinical advances were not studies conducted for clinical application. They conclude that clinical advances depend on research diversity. Murray (2002) investigates the co-evolution of science and technology regarding tissue engineering and finds that co-mingling exists in focal patent and paper networks. No star scientists have become the center in the networks. Their findings demonstrate that targeted public funding for science would face challenges of optimal distribution for promoting progress. Thus, allowing scientists to choose optimal stem cell may be rational, because the clinical application of stem cells is in its uncertain stage. Policies that target specific tools would motivate scientists to choose the latest research tools in their study. However, skewed public funding toward iPSC research in Japan differs from other targeted policies, such as for gene therapy, in that the range of target is narrow. Under such a policy, scientists may choose iPSC over other stem cells, regardless of whether the choices are optimal for their research remains unknown. The impact of excluding other candidate stem cells from research on academic performance and industry should be examined in future research.

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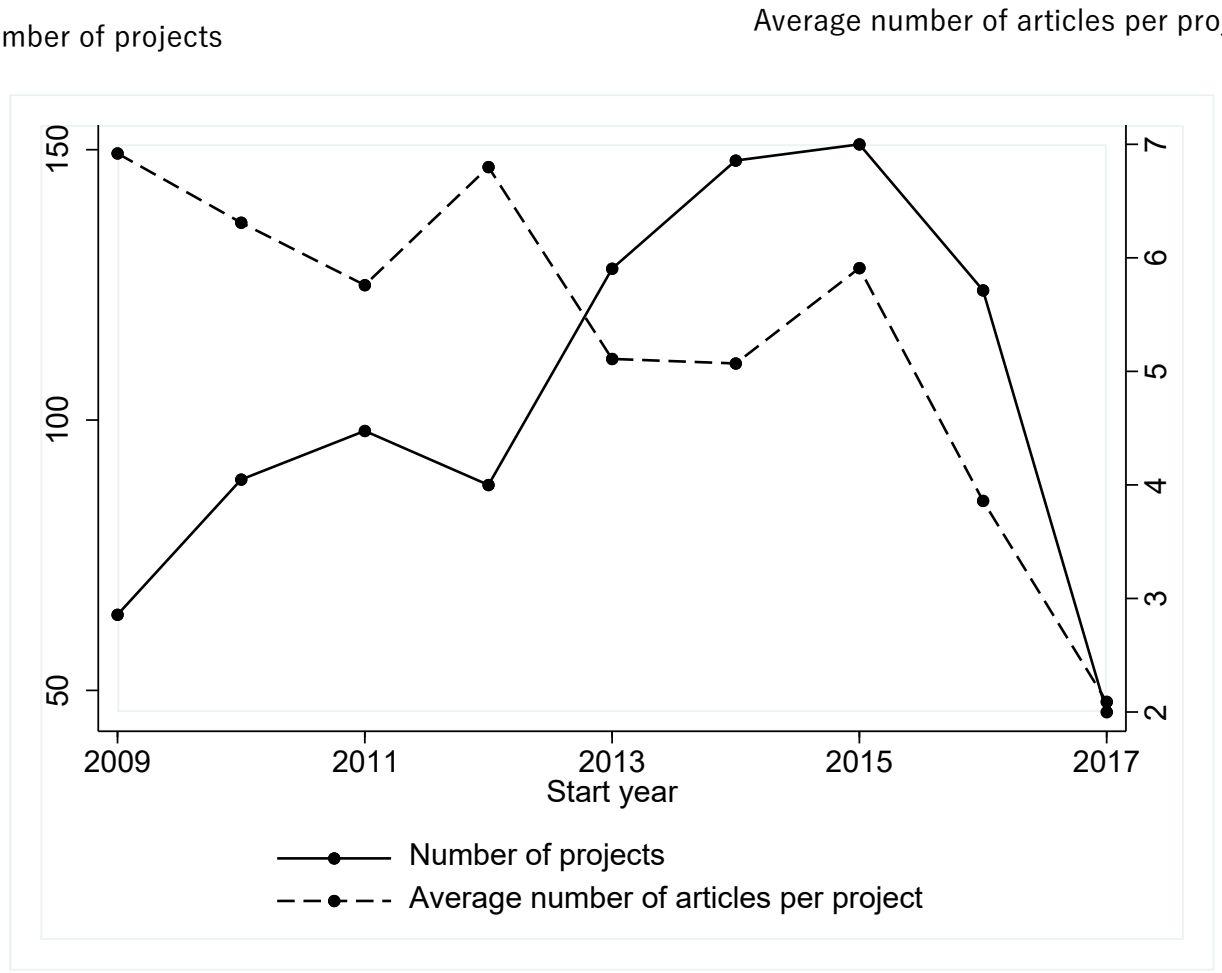
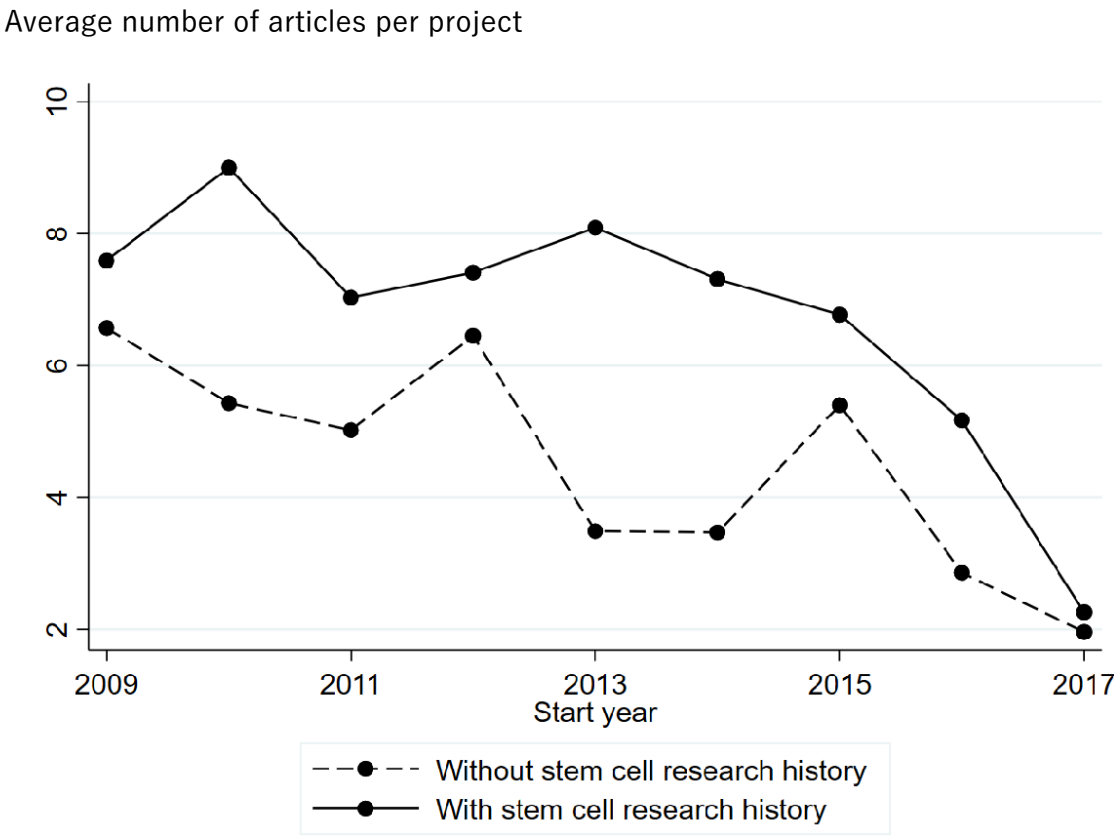
Graph 1. Number of projects and average number of articles per project and start year



Graph 2. Average number of articles per projects led by scientists with and without stem cell research history



Graph 3. Proportion of projects led by scientists with respective stem cell research history

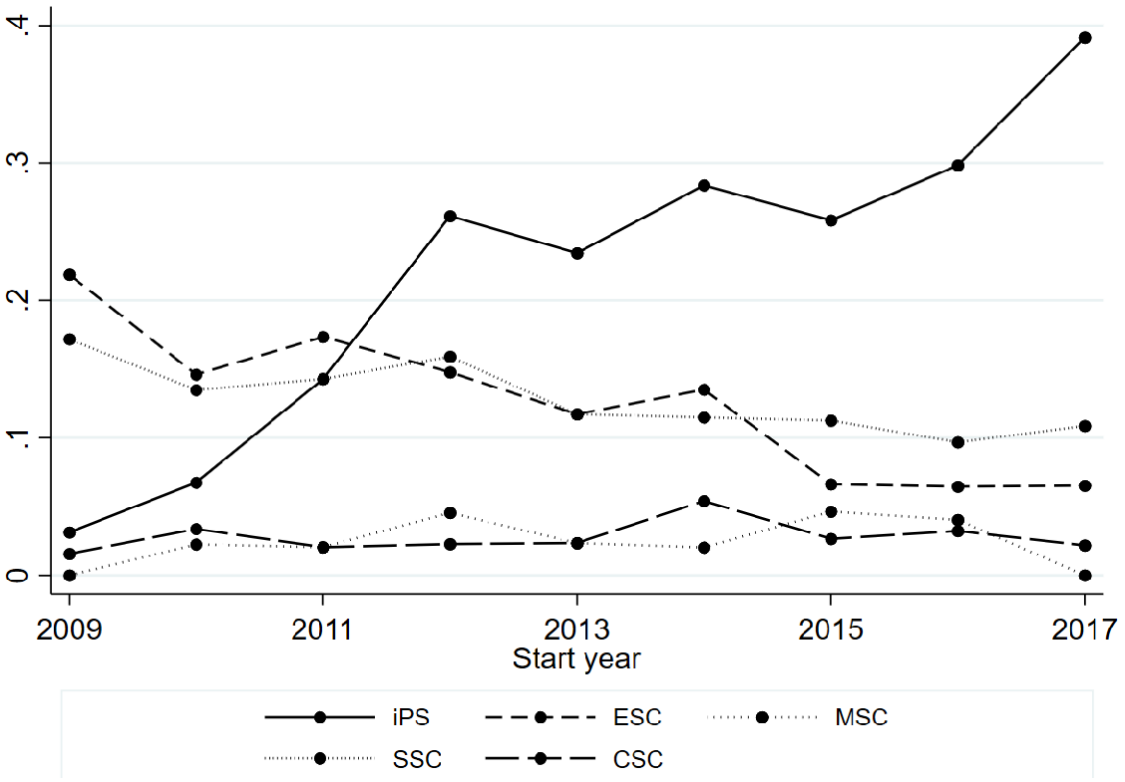


Table 1. Descriptive statistics

Variables	N	Mean	S.D.	Min.	Max.
Number of articles	936	5.38	8.19	0	119
Stem Cell	936	0.37	0.48	0	1
iPSC	936	0.23	0.42	0	1
ESC	936	0.12	0.33	0	1
MSC	936	0.03	0.16	0	1
SSC	936	0.13	0.33	0	1
CSC	936	0.03	0.17	0	1
Amount of grant (logged)	936	6.71	0.27	6.16	8.31
Specific grant for young scientists	936	0.36	0.48	0	1
Nobel Prize	936	0.64	0.48	0	1
Year 2009	936	0.07	0.25	0	1
Year 2010	936	0.10	0.29	0	1
Year 2011	936	0.10	0.31	0	1
Year 2012	936	0.10	0.29	0	1
Year 2013	936	0.14	0.34	0	1
Year 2014	936	0.16	0.37	0	1
Year 2015	936	0.16	0.37	0	1
Year 2016	936	0.13	0.34	0	1

Table 2. Correlations

Variables	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. Number of articles	-																
2. Stem Cell	0.13																
3. iPSC	0.05	0.70															
4. ESC	0.07	0.48	0.18														
5. MSC	0.04	0.22	0.03	-0.00													
6. SSC	0.14	0.49	0.19	0.29	0.07												
7. CSC	0.05	0.23	0.07	0.09	0.20	0.01											
8. Amount of grant (logged)	0.34	0.18	0.08	0.14	-0.01	0.20	0.01										
9. Specific grant for young scientists	-0.26	-0.27	-0.15	-0.16	-0.11	-0.24	-0.08	-0.32									
10. Nobel Prize	-0.09	0.06	0.17	-0.11	0.02	-0.06	0.03	0.02	0.01								
11. Year 2009	0.05	-0.02	-0.13	0.08	-0.05	0.04	-0.02	-0.00	-0.01	-0.36							
12. Year 2010	0.04	-0.08	-0.12	0.03	-0.01	0.01	0.01	-0.00	0.06	-0.43	-0.09						
13. Year 2011	0.02	-0.00	-0.07	0.06	-0.02	0.02	-0.02	-0.04	-0.03	-0.45	-0.09	-0.11					
14. Year 2012	0.06	-0.01	0.03	0.03	0.03	0.03	-0.01	0.01	-0.03	-0.43	-0.09	-0.10	-0.11				
15. Year 2013	-0.01	-0.02	0.01	-0.00	-0.01	-0.01	-0.02	0.05	-0.02	0.30	-0.11	-0.13	-0.14	-0.13			
16. Year 2014	-0.02	0.04	0.06	0.02	-0.02	-0.01	0.06	0.02	0.01	0.33	-0.12	-0.14	-0.15	-0.14	-0.17		

17. Year 2015	0.03	-0.00	0.03	-0.07	0.05	-0.02	-0.01	0.02	-0.05	0.33	-0.12	-0.14	-0.15	-0.14	-0.17	-0.19	
18. Year 2016	-0.07	0.05	0.07	-0.07	0.03	-0.03	0.01	-0.04	-0.01	0.30	-0.11	-0.13	-0.13	-0.13	-0.16	-0.17	-0.17

Table 3. Results of negative binominal regression

(1) Results for Stem cell and ESC

Independent variables	Dependent variable: Number of articles			
	Model 1	Model 2	Model 3	Model 4
Stem Cell	0.19 (0.09)*	0.35 (0.08)**		
ESC			0.14 (0.13)	0.14 (0.13)
MSC				
iPSC				
SSC				
CSC				
Amount of grant (logged)	1.01 (0.15)**	1.26 (0.15)**	1.36 (0.15)**	1.34 (0.15)**
Specific grant for young scientists	-0.76 (0.09)**			
Nobel Prize	-0.30 (0.08)**		-0.27 (0.09)**	
Year 2009		1.00 (0.25)**		0.95 (0.25)**
Year 2010		1.06 (0.24)**		1.00 (0.24)**
Year 2011		1.02 (0.23)**		1.00 (0.24)**
Year 2012		1.09 (0.24)**		1.09 (0.24)**
Year 2013		0.77 (0.23)**		0.79 (0.23)**
Year 2014		0.70 (0.23)**		0.72 (0.23)**
Year 2015		0.97 (0.22)**		0.98 (0.22)**
Year 2016		0.55 (0.23) *		0.59 (0.23)*
Constant	-4.87 (1.00)**	-7.86 (1.04)**	-7.35 (1.04)**	-8.29 (1.05)**
N	936	936	936	936
Log likelihood	-2462.71	-2484.87	-2502.93	-2492.81
LR χ^2	185.70**	141.38**	105.25**	125.50**

**P<0.01, *P<0.5

S.D. is in parenthesis.

(2) Results for MSC and iPSC

Independent variables	Dependent variable: Number of articles			
	Model 5	Model 6	Model 7	Model 8
Stem Cell				
ESC				
MSC	0.48 (0.25)+	0.42 (0.25)+		
iPSC			0.18 (0.10)+	0.20 (0.10)*
SSC				
CSC				
Amount of grant (logged)	1.38 (0.15)**	1.37 (0.15)**	1.35 (0.15)**	1.33 (0.15)**
Specific grant for young scientists				
Nobel Prize	-0.29 (0.09)**		-0.31 (0.09)**	
Year 2009		0.98 (0.25)**		1.04 (0.25)**
Year 2010		1.01 (0.24)**		1.08 (0.24)**
Year 2011		1.02 (0.24)**		1.07 (0.24)**
Year 2012		1.08 (0.24)**		1.11 (0.24)**
Year 2013		0.77 (0.23)**		0.82 (0.23)**
Year 2014		0.73 (0.22)**		0.74 (0.23)**
Year 2015		0.96 (0.22)**		1.01 (0.22)**
Year 2016		0.57 (0.23)*		0.60 (0.23)*
Constant	-7.52 (1.04)**	-8.45 (1.05)**	-7.31 (1.03)**	-8.29 (1.04)**
N	936	936	936	936
Log likelihood	-2501.39	-2491.77	-2501.97	-2491.38
LR χ^2	108.33***	127.58**	107.19**	128.36**

**P<0.01, *P<0.5, +P<0.1

S.D. is in parenthesis.

(3) Results for SSC and CSC

Independent variables	Dependent variable: Number of articles			
	Model 9	Model 10	Model 11	Model 12
Stem Cell				
ESC				
MSC				
iPSC				
SSC	0.29 (0.12)*	0.30 (0.12)*		
CSC			0.41 (0.24)+	0.46 (0.24)+
Amount of grant (logged)	1.30 (0.16)**	1.28 (0.15)**	1.37 (0.15) **	1.36 (0.15)**
Specific grant for young scientists				
Nobel Prize	-0.27 (0.09)**		-0.28 (0.09)**	
Year 2009		0.98 (0.25)**		0.99 (0.25)**
Year 2010		1.01 (0.24)**		1.02 (0.24)**
Year 2011		1.01 (0.24)**		1.01 (0.24)**
Year 2012		1.11 (0.24)**		1.10 (0.24)**
Year 2013		0.82 (0.23)**		0.81 (0.23)**
Year 2014		0.75 (0.23)**		0.73 (0.23)**
Year 2015		0.99 (0.22)**		1.00 (0.22)**
Year 2016		0.59 (0.23)*		0.58 (0.23)*
Constant	-7.00 (1.04)**	-7.89 (1.05)**	-7.44 (1.03)**	-8.40 (1.04)**
N	936	936	936	936
Log likelihood	-2500.66	-2490.29	-2501.87	-2491.28
LR χ^2	109.80**	130.55**	107.37**	128.56**

**P<0.01, *P<0.5, +P<0.1

S.D. is in parenthesis.

Table 4. Comparison of the impact of stem cell research history before and after the 2012 Nobel Prize

Independent variables	Dependent variable: Number of articles											
	Model 13	Model 14	Model 15	Model 16	Model 17	Model 18	Model 19	Model 20	Model 21	Model 22	Model 23	Model 24
	Stem cell		ESC		MSC		iPSC		SSC		CSC	
	before	after	before	after	before	after	before	after	before	after	before	after
Stem Cell	0.11 (0.13)	0.42 (0.11)**										
ESC			0.09 (0.17)	0.18 (0.18)								
MSC					-0.01 (0.42)	0.63 (0.31)*						
iPSC							0.02 (0.19)	0.22 (0.12)+				
SSC									0.24 (0,17)	0.33 (0.17)+		
CSC											0.67 (0.40)+	0.28 (0.30)
Amount of grant (logged)	1.36 (0.22)**	1.22 (0.21)**	1.36 (0.22)**	1.35 (0.21)**	1.38 (0.22)**	1.37 (0.21)**	1.38 (0.22)**	1.31 (0.21)**	1.34 (0.22)**	1.26 (0.22)**	1.38 (0.22)**	1.35 (0.21)**
Constant	-7.39 (1.48)**	-6.86 (1.41)**	-7.40 (1.48)**	-7.54 (1.42)**	-7.48 (1.48)**	-7.72 (1.42)**	-7.48 (1.47)**	-7.37 (1.40)**	-7.28 (1.47)**	-6.96 (1.45)**	-7.56 (1.46)**	-7.58 (1.42)**
N	333	603	333	603	333	603	333	603	333	603	333	603
Log likelihood	-940.80	-1553.64	-941.01	-1560.38	-941.17	-1558.39	-941.16	-1559.11	-940.15	-1558.98	-939.47	-1560.41
LR χ^2	48.09**	62.59**	47.69**	49.12**	47.36**	53.09**	47.37**	51.64**	49.39**	51.91**	50.76**	49.04**

**P<0.01, *P<0.5, +P<0.1

S.D. is in parenthesis.