Overview

The National Human Genome Research Institute (NHGRI) Ethical, Legal and Social Implications (ELSI) Research Program frequently receives requests for examples of funded grant applications. Several investigators and their organizations agreed to let excerpts of their ELSI grant applications be posted online.

Acknowledgement

We are grateful to the investigators and their institutions for allowing us to provide this important resource to the community. To maintain confidentiality, we have redacted some information from these documents (e.g., budgets, social security numbers, home addresses, introduction to revised application), where applicable. We do not include other SF 424 (R&R) forms or requisite information found in the full grant application (e.g., budgets, biographical sketches, letters of recommendation or letters of support). NIH grant formats or rules may have changed since these applications were prepared; therefore, applicants should always follow the application format instructions included in the funding announcement.

PI: **Prince, Anya**	Title: Use of Genetic Information by Life, Long-term Care, and Disability Insurers: Exploring International Lessons, the Domestic Legal Landscape, and Options for U.S. Policy	
Received: 02/11/2015	FOA: PA15-083	Council: 10/2015
Competition ID: FORMS-C	FOA Title: NIH PATHWAY TO INDEPENDENCE AWARD (PARENT K99/R00)	
1 K99 HG008819-01	Dual: AG,NR	Accession Number: 3789133
IPF: 578206	Organization: UNIV OF NORTH CAROLINA CHAPEL HILL	
Former Number:	Department: Social Medicine	
IRG/SRG: SEIR	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: 84,474 Year 2: 86,710 Year 3: 163,816 Year 4: 163,816 Year 5: 163,816	Animals: N Humans: Y Clinical Trial: N Current HS Code: HESC: N Evaluative Info	New Investigator: Early Stage Investigator:
Senior/Key Personnel:	*Organization:*	*Role Category:*
Anya Prince	The University of North Carolina at Chapel Hill	PD/PI
Gail Henderson Ph.D	The University of North Carolina at Chapel Hill	Other Professional-Mentor
Debra Skinner Ph.D	The University of North Carolina at Chapel Hill	Other Professional-Co-Mentor
Mark Hall	Wake Forest University	Other Professional-Co-Mentor

Reference Letters

Reference name

Reference name

Reference name

Additions for Review

Accepted Publication list of new publications

OMB Number: 4040-0001
Expiration Date: 06/30/2016

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	State Application Identifier

1. TYPE OF SUBMISSION*
❍ Pre-application ❍ Application ● Changed/Corrected Application

4.a. Federal Identifier

b. Agency Routing Number

2. DATE SUBMITTED | **Application Identifier**

c. Previous Grants.gov Tracking Number
GRANT11832866

5. APPLICANT INFORMATION **Organizational DUNS*:** 608195277

Legal Name*: The University of North Carolina at Chapel Hill
Department: Office of Sponsored Research
Division: Research
Street1*: 104 Airport Drive, suite 2200, CB#1350
Street2:
City*: Chapel Hill
County: Orange
State*: NC: North Carolina
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 24599-1350

Person to be contacted on matters involving this application
Prefix: First Name*: Kim Middle Name: Last Name*: Jones Suffix:
Position/Title: Grants Analyst, Sponsored Programs Office
Street1*: 1140 Bioinformatics Bldg., CB9525
Street2: 130 Mason Farm Road
City*: Chapel Hill
County: Orange
State*: NC: North Carolina
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 27599-9525
Phone Number*: 919-962-3950 Fax Number: Email: grants@unc.edu

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** 1566001393A1

7. TYPE OF APPLICANT* H: Public/State Controlled Institution of Higher Education

Other (Specify):
Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*
● New ❍ Resubmission
❍ Renewal ❍ Continuation ❍ Revision

If Revision, mark appropriate box(es).
❍ A. Increase Award ❍ B. Decrease Award ❍ C. Increase Duration
❍ D. Decrease Duration ❍ E. Other *(specify)* :

Is this application being submitted to other agencies?* ❍Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY*
National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Use of Genetic Information by Life, Long-term Care, and Disability Insurers: Exploring International Lessons, the Domestic Legal Landscape, and Options for U.S. Policy

12. PROPOSED PROJECT
Start Date* Ending Date*
09/01/2015 08/31/2020

13. CONGRESSIONAL DISTRICTS OF APPLICANT
NC-004

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: Ms. First Name*: Anya Middle Name: Last Name*: Prince Suffix:

Position/Title: Postdoctoral Research Fellow
Organization Name*: The University of North Carolina at Chapel Hill
Department: Social Medicine
Division: School of Medicine
Street1*: 333 South Columbia Street
Street2: 343 MacNider Hall
City*: Chapel Hill
County: Orange
State*: NC: North Carolina
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 24599-7240
Phone Number*: 919-962-8493 Fax Number: 919-966-7499 Email*: anya_prince@med.unc.edu

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested*	$931,879.00
b. Total Non-Federal Funds*	$0.00
c. Total Federal & Non-Federal Funds*	$931,879.00
d. Estimated Program Income*	$0.00

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:

DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR

○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: Dr. First Name*: Barbara Middle Name: Last Name*: Entwisle Suffix: Ph.D

Position/Title*: Vice Chancellor for Research
Organization Name*: The University of North Carolina at Chapel Hill
Department: Office of Sponsored Research
Division: Research
Street1*: 104 Airport Drive, suite 2200, CB#1350
Street2:
City*: Chapel Hill
County: Orange
State*: NC: North Carolina
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 24599-1350
Phone Number*: 919-966-3411 Fax Number: 919-966-3352 Email*: resadminosr@unc.edu

Signature of Authorized Representative*
Kim Jones

Date Signed*
02/11/2015

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:1250-21_Cover_Letter.pdf

424 R&R and PHS-398 Specific Table Of Contents

OMB Number: 4040-0010
Expiration Date: 06/30/2016

Project/Performance Site Location(s)

Project/Performance Site Primary Location

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	The University of North Carolina at Chapel Hill
Duns Number:	6081952770000
Street1*:	104 Airport Drive, suite 2200, CB#1350
Street2:	
City*:	Chapel Hill
County:	Orange
State*:	NC: North Carolina
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	27599-1350
Project/Performance Site Congressional District*:	NC-004

File Name

Additional Location(s)

Funding Opportunity Number: PA-15-083. Received Date: 2015-02-11T15:56:35.000-05:00

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ● **Yes** ○ **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ● No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6

If NO, is the IRB review Pending? ● **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number 00004801

2. Are Vertebrate Animals Used?* ○ **Yes** ● **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ● **Yes** ○ **No**

6.a. If yes, identify countries: Canada and three additional to-be-determined countries,

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	1242-7_Project_Summary_Abstract.pdf
8. Project Narrative*	1243-8_Project_Narrative.pdf
9. Bibliography & References Cited	1244-9_Bibliography.pdf
10.Facilities & Other Resources	1245-10_Facilities.pdf
11.Equipment	1246-11_Equipment.pdf
12. Other Attachments	1247-12a_Referee_List.pdf 1248-12b_Letter_on_Law_School_Research_Tenure.pdf 1249-12c_Foreign_Justification.pdf

Funding Opportunity Number: PA-15-083. Received Date: 2015-02-11T15:56:35.000-05:00

Project Summary/Abstract

Use of Genetic Information by Life, Long-term Care, and Disability Insurers: Exploring International Lessons, the Domestic Legal Landscape, and Options for U.S. Policy

This project employs multiple methods and a transdisciplinary approach to explore policy options for US federal and state governments seeking to address how life, long-term care, and disability insurers use genetic information. The analysis will focus on legal standards of actuarial justification, that is, the requirement that insurers must show a statistical correlation between a risk factor and increased cost in order to use that factor in an underwriting decision such as a policy denial or an increased premium. Policies in this area can significantly affect the heath of individuals in two ways. First, barriers of access to life, long-term care, or disability insurance can threaten economic stability of individuals and families, leading to inability to pay for healthcare or other necessities. Second, fear of genetic discrimination may prevent individuals from undergoing predictive genetic testing, testing that could provide clinically relevant information to help prevent or mitigate future disease. This project has two primary goals: 1) to systematically examine the legal and policy landscape of life, long-term care, and disability insurer use of genetic information in the US and internationally; and 2) to offer a variety of policy options for US federal and state governments that seek to address genetic discrimination in this area. To meet these goals, I propose three specific aims.

Aim 1 employs a case study methodology to explore the policy mechanisms that four countries outside the US have utilized to address insurer use of genetic information, with particular focus on how these policies use and define standards of actuarial justification. For each case study I will conduct a search and analysis of relevant policy documents as well as conduct and analyze targeted, in-depth interviews with key stakeholders such as academic/policy experts, government officials, advocacy group representatives, and insurance representatives.

Aim 2 interrogates how existing US state actuarial justification laws have been interpreted and enforced in the context of genetic information through two sub-aims. Aim 2a utilizes survey methodology to empirically examine how US state insurance commissioners are interpreting and enforcing state actuarial laws. Aim 2b employs legal analysis of statutes, regulations, and applicable state law to evaluate how states have legally defined and deployed actuarial justification standards. The survey responses of Aim 2a will inform the legal analysis regarding how existing legislation may be enforced or interpreted.

Aim 3 undertakes policy analysis of the legislative and regulatory options available to US governments at the state and federal level. Through policy analysis and critique, conclusions drawn from Aims 1 and 2, and feedback from a policy-experts, Aim 3 will provide policy options to address life, long-term care, and disability insurer use of genetic information and to address the threshold evidence levels needed to meet actuarial standards in this area. This project and the final policy recommendations directly support an identified ELSI research priority of the NHGRI regarding life, long-term care, and disability insurer use of genetic information.

Project Narrative

As clinicians and researchers explore how genomic sequencing can be utilized to prevent or mitigate genetic conditions and diseases, many individuals who are expected to benefit from these findings remain fearful of how insurers not currently included under federal genetic discrimination legislation can use their sequencing and test results, with potentially harmful outcomes. Through exploration of both the US and international context, this project seeks to better understand the ways that life, long-term care, and disability insurers can legally use genetic information, with particular focus on legal standards of actuarial justification. By providing policy recommendations to address possible discrimination, this project addresses an important NHGRI legal, regulatory, and public policy research priority to investigate the use of genetic information by life, disability, and long-term care insurance companies, determination of actuarial risk, and the impact of state laws.

Bibliography

1. Actuarial Standards Board. (2005). *Actuarial Standard of Practice (ASOP) No. 12: Risk Classification (for All Practice Areas)*.
2. Allain, D. C., Friedman, S., & Senter, L. (2012). Consumer awareness and attitudes about insurance discrimination post enactment of the Genetic Information Nondiscrimination Act. *Familial Cancer, 11*(4), 637-644. doi: 10.1007/s10689-012-9564-0, PMID: 22890887.
3. Anderlik, M. R., & Rothstein, M. A. (2001). Privacy and confidentiality of genetic information: what rules for the new science? *Annual Review of Genomics and Human Genetics, 2*(1), 401-433. PMID: 11701656.
4. *Ashcroft, R. (2007). Should genetic information be disclosed to insurers? No. *BMJ, 334*(7605), 1197-1197. doi: 10.1136/bmj.39216.425231.AD, PMCID: 1889956.
5. *Atkinson, P., Glasner, P., & Lock, M. (2009). *The Handbook of Genetics & Society: Mapping the New Genomic Era*: Routledge.
6. Australian Law Reform Commission (ALRC). (2003). *Essentially Yours--The Protection of Human Genetic Information in Australia, Volume 1 and Volume 2*. Report 96.
7. Avraham, R., Logue, K. D., & Schwarcz, D. B. (2014). Understanding insurance anti-discrimination laws. *Southern California Law Review, 87*, 195-274.
8. Baker, T. (2002). Containing the promise of insurance: adverse selection and risk classification. *Connecticut Insurance Law Journal, 9*, 371-398.
9. *Barlow-Stewart, K., Taylor, S. D., Treloar, S. A., Stranger, M., & Otlowski, M. (2009). Verification of consumers' experiences and perceptions of genetic discrimination and its impact on utilization of genetic testing. *Genetics in Medicine, 11*(3), 193-201. doi: 10.1097/GIM.0b013e318194ee75, PMID: 19287242.
10. Cal-GINA. (2011). Unruh Civil Rights Act § 51.
11. Cancer Legal Resource Center (CLRC). (2012). *The Healthcare Professional Manual: A Legal Resource Guide for Oncology Heatlh Care Professionals*. Los Angeles, CA.
12. Caulfield, T., Chandrasekharan, S., Joly, Y., & Cook-Deegan, R. (2013). Harm, hype and evidence: ELSI research and policy guidance. *Genome Medicine, 5*(3), 21-27. doi: 10.1186/gm425, PMCID: 3707044.
13. Center for Responsible Genetics (CRG). (2014). State Laws on Genetic Privacy, Consumer Genetic Privacy Manual.
14. Chabner v. United of Omaha Life Ins. Co., 225 F.3d 1042 (9th Cir. 2000).
15. *Daykin, C. D., Akers, D. A., Macdonald, A. S., McGleenan, T., Paul, D., & Turvey, P. J. (2003). Genetics and insurance–some social policy issues. *British Actuarial Journal, 9*(04), 787-830.
16. Dodge, J. H., & Christianson, D. J. (2007). Genetic testing and disability insurance: An alternative opinion. *The Journal of Law, Medicine & Ethics, 35*(s2), 33-35. PMID: 17543054.
17. *Dubois, M. (2011). Insurance and prevention: ethical aspects. *The Journal of Primary Prevention, 32*(1), 3-15.
18. Evans, J. P., Skrzynia, C., & Burke, W. (2001). The complexities of predictive genetic testing. *BMJ, 322*, 1052-1056. PMCID: 1120190.
19. Feldman, E. A. (2012). The Genetic Information Nondiscrimination Act (GINA): Public policy and medical practice in the age of personalized medicine. *Journal of General Internal Medicine, 27*(6), 743-746. PMCID: 3358381.
20. Gruber, J. (2014, April 14). Guarantee Privacy to Ensure Proper Genetic Treatment. *New York Times*. Retrieved from http://www.nytimes.com/roomfordebate/2014/04/14/dna-and-insurance-fate-and-risk/guarantee-privacy-to-ensure-proper-genetic-treatment.
21. Guest, G., Namey, E. E., & Mitchell, M. L. (2012). *Collecting qualitative data: A field manual for applied research*: Sage.
22. Green, R. C., Lautenbach, D., & McGuire, A. L. (2015). GINA, Genetic Discrimination, and Genomic Medicine. *New England Journal of Medicine, 372*(5), 397-399. doi: 10.1056/NEJMp1404776.
23. Haidle, J. L. (2014, April 14). Genetic Test Results Are Not Always What They Seem. *New York Times*. Retrieved from http://www.nytimes.com/roomfordebate/2014/04/14/dna-and-insurance-fate-and-risk/genetic-test-results-are-not-always-what-they-seem.

24. Hall, M. A., & Rich, S. S. (2000a). Genetic privacy laws and patients' fear of discrimination by health insurers: The view from genetic counselors. *The Journal of Law, Medicine & Ethics, 28*(3), 245-257. PMID: 1121037.
25. Hall, M. A., & Rich, S. S. (2000b). Laws Restricting Health Insurers' Use of Genetic Information: Impact on Genetic Discrimination. *American Journal of Human Genetics, 66*, 293-307. PMCID: 1288333.
26. Hall, M. A., & Rich, S. S. (2000c). Patients' fear of genetic discrimination by health insurers: the impact of legal protections. *Genetics in Medicine, 2*(4), 214-221. PMID: 11252705.
27. Her Majesty's Government (HMG) & the Association of British Insurers. (2011). *Concordat and Moratorium on Genetics and Insurance*.
28. Holmes, E. M. (1996). Solving the insurance/genetic fair/unfair discrimination dilemma in light of the Human Genome Project. *Kentucky Law Journal, 85*(503), 506-664.
29. Hudson, K. L., Holohan, M. K., & Collins, F. S. (2008). Keeping pace with the times—the Genetic Information Nondiscrimination Act of 2008. *New England Journal of Medicine, 358*(25), 2661-2663. PMID: 18565857.
30. *Huijgen, R., Homsma, S. J. M., Hutten, B. A., Kindt, I., Vissers, M. N., Kastelein, J. J. P., & van Rijckevorsel, J. L. A. (2012). Improved access to life insurance after genetic diagnosis of familial hypercholesterolaemia: cross-sectional postal questionnaire study. *European Journal of Human Genetics, 20*(7), 722-728. doi: 10.1038/ejhg.2012.5, PMCID: 3376271.
31. *Janssens, A. C. J. W., & Khoury, M. J. (2012). Predictive value of testing for multiple genetic variants in multifactorial diseases: implications for the discourse on ethical, legal and social issues. *Italian Journal of Public Health, 3*(3-4).
32. Jha, S. (2012). Punishing the lemon: the ethics of actuarial fairness. *Journal of the American College of Radiology, 9*(12), 887-893. doi: 10.1016/j.jacr.2012.09.012, PMID: 23206646.
33. *Joly, Y. (2006). Life Insurers' Access to Genetic Information: A Way Out of the Stalemate? *Health Law Review, 14*(3), 14-21.
34. *Joly, Y., Braker, M., & Le Huynh, M. (2010). Genetic discrimination in private insurance: global perspectives. *New Genetics and Society, 29*(4), 351-368. doi: 10.1080/14636778.2010.528189.
35. *Joly, Y., Burton, H., Knoppers, B. M., Feze, I. N., Dent, T., Pashayan, N., Chowdhury, S., Foulkes, W., Hall, A., Hamet, P., Kirwan, N., Macdonald, A., Simard, J., & Van Hoyweghen, I. (2014). Life insurance: genomic stratification and risk classification. *European Journal of Human Genetics, 22*(5), 575-579. doi: 10.1038/ejhg.2013.228, PMCID: 3992580.
36. *Joly, Y., Ngueng Feze, I., & Simard, J. (2013). Genetic discrimination and life insurance: a systematic review of the evidence. *BMC Medicine, 11*, 25. doi: 10.1186/1741-7015-11-25, PMCID: 3606414.
37. *Keogh, L. A., & Otlowski, M. F. A. (2013). Life insurance and genetic test results: a mutation carrier's fight to achieve full cover. *Medical Journal of Australia, 199*(5), 363-366. doi: 10.5694/mja13.10202, PMID: 23992195.
38. King, N., & Horrocks, C. (2010). *Interviews in qualitative research*: Sage.
39. Klitzman, R. (2010). Views of discrimination among individuals confronting genetic disease. *Journal of Genetic Counseling, 19*(1), 68-83. doi: 10.1007/s10897-009-9262-8, PMCID: 3152486.
40. Klitzman, R., Appelbaum, P. S., & Chung, W. K. (2014). Should Life Insurers Have Access to Genetic Test Results? *JAMA, 312*(18), 1855-1856. PMID: 25387181.
41. *Knoppers, B. M., Godard, B., & Joly, Y. (2004a). A comparative international overview. In M. A. Rothstein (Ed.), *Genetics and life insurance: medical underwriting and social policy* (pp. 173-194).
42. *Knoppers, B. M., & Joly, Y. (2004b). Physicians, genetics and life insurance. *Canadian Medical Association Journal, 170*(9), 1421-1423. doi: 10.1053/cmaj.1040127, PMID: 15111477.
43. Laedtke, A. L., O'Neill, S. M., Rubinstein, W. S., & Vogel, K. J. (2012). Family physicians' awareness and knowledge of the Genetic Information Non-Discrimination Act (GINA). *Journal of Genetic Counseling, 21*(2), 345-352. doi: 10.1007/s10897-011-9405-6, PMID: 21927977.
44. Landes, X. (2014). How Fair Is Actuarial Fairness? *Journal of Business Ethics*, 1-15.
45. *Lemke, T. (2013). *Perspectives on Genetic Discrimination* (Vol. 100): Routledge.
46. *Lemmens, T. (2003). Genetics and insurance discrimination: Comparative legislative, regulatory and policy developments and Canadian options. *Health Law Journal*, 41-86.
47. *Lemmens, T., Joly, Y., & Knoppers, B. M. (2004). Genetics and life insurance: a comparative analysis.
48. *Lemmens, T., Pullman, D., & Rodal, R. (2010). Revisiting genetic discrimination issues in 2010: policy options for Canada: Genome Canada.

49. *Liukko, J. (2010). Genetic discrimination, insurance, and solidarity: an analysis of the argumentation for fair risk classification. *New Genetics and Society, 29*(4), 457-475.
50. *Macdonald, A., & Tapadar, P. (2010). Multifactorial genetic disorders and adverse selection: Epidemiology meets economics. *Journal of Risk and Insurance, 77*(1), 155-182.
51. *Macdonald, A., & Yu, F. (2011). The Impact of Genetic Information on the Insurance Industry: Conclusions from the 'Bottom-Up'Modelling Programme. *Astin Bulletin, 41*(02), 343-376.
52. *MacDonald, A. S. (2002). Genetics and health costs: some actuarial models. *Law, Probability and Risk, 1*, 97-118.
53. *Macdonald, A. S., Waters, H. R., & Wekwete, C. T. (2003). The genetics of breast and ovarian cancer II: A model of critical illness insurance. *Scandinavian Actuarial Journal, 2003*(1), 28-50.
54. McEwen, J. E., McCarty, K., & Reilly, P. R. (1992). A Survey of State Insurance Commissioners Concerning Genetic Testing and Life Insurance. *American Journal of Human Genetics, 51*, 785-792. PMCID: 1682778.
55. McEwen, J. E., McCarty, K., & Reilly, P. R. (1993). A survey of medical directors of life insurance companies concerning use of genetic information. *American Journal of Human Genetics, 53*(1), 33. PMCID: 1682223.
56. McGuire, A. L., & Majumder, M. A. (2009). Two cheers for GINA. *Genome Medicine, 1*(1), 6. doi: 10.1186/gm6, PMCID: 2651591.
57. *Mittra, J. (2007). Predictive Genetic Information and Access to Life Assurance: The Poverty of 'Genetic Exceptionalism'. *BioSocieties, 2*(3), 349-373. doi: 10.1017/s1745855207005789.
58. *Morris, L. A. (2010). Life insurance and genetic tests: Risks for insurers and society. *Health, Risk & Society, 12*(3), 251-270.
59. *Moultrie, T. A., & Thomas, R. G. (1997). The right to underwrite? An actuarial perspective with a difference. *Journal of Actuarial Practice, 5*(1), 125-146.
60. National Association of Insurance Commissioners (NAIC). (2011). *State Insurance Regulation*.
61. National Conference of State Legislatures. (2008). *Genetics and Life, Disability, and Long-term Care Insurance*.
62. National Human Genome Research Institute (NHGRI). (2014). *ELSI Research Priorities and Possible Research Topics.*
63. Ostrer, H., Allen, W., Crandall, L. A., Moseley, R. E., Dewar, M. A., Nye, D., & McCrary, S. (1993). Insurance and genetic testing: where are we now? *American Journal of Human Genetics, 52*(3), 565. PMCID: 1682164.
64. *Otlowski, M., Taylor, S., & Bombard, Y. (2012). Genetic discrimination: international perspectives. *Annual Review of Genomics and Human Genetics, 13*, 433-454. doi: 10.1146/annurev-genom-090711-163800, PMID: 22607273.
65. Oregon Revised Statutes (ORS) § 746.135 (2001).
66. Parkman, A. A., Foland, J., Anderson, B., Duquette, D., Sobotka, H., Lynn, M., Nottingham, S., Dotson, W. D., Kolor, K., & Cox, S. L. (2014). Public Awareness of Genetic Nondiscrimination Laws in Four States and Perceived Importance of Life Insurance Protections. *Journal of Genetic Counseling*, 1-10. doi: 10.1007/s10897-014-9771-y, PMID: 25242499.
67. Peikoff, K. (2014, April 7). Fearing Punishment for Bad Genes. *The New York Times*. Retrieved from http://www.nytimes.com/2014/04/08/science/fearing-punishment-for-bad-genes.html?_r=0.
68. Peshkin, B. N., & Burke, W. (2013). Bioethics of genetic testing for hereditary breast cancer. *Hereditary Breast Cancer*, 35.
69. Prince, A. E. R. (2013). Comprehensive Protection of Genetic Information-One Size Privacy of Property Models May Not Fit All. *Brooklyn Law Review, 79*, 175-227.
70. *Pullman, D., & Lemmens, T. (2010). Keeping the GINA in the bottle: assessing the current need for genetic non-discrimination legislation in Canada. *Open Medicine, 4*(2), e95. PMCID: 3116686.
71. *Quinn, G., de Paor, A., & Blanck, P. (2014). *Genetic Discrimination: Transatlantic Perspectives on the Case for a European Level Legal Response*: Routledge.
72. *Radetzki, M., Radetzki, M., & Juth, N. (2003). *Genes and insurance: Ethical, legal and economic issues*: Cambridge University Press.
73. Ragin, C. C. (1999). The distinctiveness of case-oriented research. *Health Services Research, 34*(5 Pt 2), 1137.
74. Ragin, C. C. (2014). *The comparative method: Moving beyond qualitative and quantitative strategies*: Univ of California Press.

75. Randall, S. (1998). Insurance Regulation in the United States: Regulatory Federalism and the National Association of Insurance Commissioners. *Florida State University Law Review, 26*(3), 625-699.
76. *Rennie, S. (2013). Genetic Non-Discrimination Act: New Bill Would Stop Discrimination By Insurance Firms. *Huffington Post Canada*. Retrieved from http://www.huffingtonpost.ca/2013/04/17/genetic-non-discrimination-act-bill_n_3102527.html.
77. Rothstein, M. A. (1997). *Genetic secrets: protecting privacy and confidentiality in the genetic era*: Yale University Press.
78. Rothstein, M. A. (2004). *Genetics and life insurance: Medical underwriting and social policy*: MIT Press.
79. Rothstein, M. A. (2007). Genetic exceptionalism and legislative pragmatism. *Journal of Law, Medicine & Ethics, 35*(s2), 59-65. PMID: 17543059.
80. Rothstein, M. A., & Joly, Y. (2009). Genetic information and insurance underwriting. *The Handbook of Genetics & Society: Mapping the New Genomic Era*, 127.
81. *Soini, S. (2012). Genetic testing legislation in Western Europe—a fluctuating regulatory target. *Journal of community genetics, 3*(2), 143-153. doi: 10.1007/s12687-012-0078-0, PMCID: 3312949.
82. Stake, R. E. (2013). *Multiple case study analysis*: Guilford Press.
83. *Taylor, S. D., Otlowski, M. F., Barlow‐Stewart, K. K., Treloar, S. A., Stranger, M., & Chenoweth, K. (2004). Investigating genetic discrimination in Australia: opportunities and challenges in the early stages. *New Genetics and Society, 23*(2), 225-239. PMID: 15460616.
84. *Thomas, R. G. (2012). Genetics and insurance in the United Kingdom 1995–2010: the rise and fall of “scientific” discrimination. *New Genetics and Society, 31*(2), 203-222.
85. Unfair Trade Practices Act (UTPA). (2004). Model Law.
86. Van de Ven, A. H., Polley, D. E., Garud, R., & Venkataraman, S. (1999). *The innovation journey*: Oxford University Press New York.
87. *Van Hoyweghen, I. (2007). *Risks in the making: travels in life insurance and genetics*: Amsterdam University Press.
88. *Van Hoyweghen, I., Horstman, K., & Schepers, R. (2005). ‘Genetics is not the issue’: Insurers on genetics and life insurance. *New Genetics and Society, 24*(1), 79-98. PMID: 16552918.
89. *Van Hoyweghen, I., & Rebert, L. (2012). Your genes in insurance: from genetic discrimination to genomic solidarity. *Personalized Medicine, 9*(8), 871-877. doi: 10.2217/pme.12.96.
90. *Varga, O., Soini, S., Kääriäinen, H., Cassiman, J.-J., Nippert, I., Rogowski, W., Nys, H., Kristoffersson, U., Schmidtke, J., & Sequeiros, J. (2012). Definitions of genetic testing in European legal documents. *Journal of Community Genetics, 3*(2), 125-141. doi: 10.1007/s12687-012-0077-1, PMCID: 3312943.
91. Vermont Statutes Annotated (VSA). (1997). tit. 18, § 9334.
92. Viswanathan, K. S., Lemaire, J., Withers, K., Armstrong, K., Baumritter, A., Hershey, J. C., Pauly, M. V., & Asch, D. A. (2007). Adverse selection in term life insurance purchasing due to the BRCA1/2 genetic test and elastic demand. *Journal of Risk and Insurance, 74*(1), 65-86.
93. Wolf, S. M., & Kahn, J. P. (2007). Genetic testing and the future of disability insurance: ethics, law & policy. *The Journal of Law, Medicine & Ethics, 35*(s2), 6-32. PMID: 17543053.
94. Yin, R. (2003). Case study research: Design and methods. *Sage Publications, Inc, 5*, 11.

* First author is an international scholar.

Facilities and Other Resources

The University of North Carolina at Chapel Hill

Founded in 1792, the University of North Carolina is the oldest public university in the United States. The University of North Carolina at Chapel Hill (UNC) is the flagship campus for the 16-campus University of North Carolina system with more than 29,000 students, six professional schools, and five health affairs schools. These include Business, Law, Education, Journalism, Social Work, Information and Library Sciences, and the Schools of Dentistry, Medicine, Nursing, Pharmacy and Public Health. UNC is a research-intensive institution and consistently ranks among the top U.S. public universities in research support. In fiscal 2014 its researchers attracted more than $792 million, a direct reflection of the quality of the research the faculty are conducting and the excellence of the infrastructure that supports their research. UNC has spearheaded a commitment to expanding and enriching resources available to researchers while emphasizing the collaborative links between basic scientists at the bench, clinicians in the hospital, and social science and bioethical researchers. This general atmosphere, and specific resources provided by departments and research centers make UNC an exhilarating place to conduct research.

The following is a list of relevant resources that will be available to this K99/R00, “Use of Genetic Information by Life, Long-term Care, and Disability Insurers: Exploring International Lessons, the Domestic Legal Landscape, and Options for U.S. Policy”. The UNC web site (www.unc.edu) provides a rich description of virtually every resource on campus.

School of Medicine

The UNC School of Medicine has a record of maintaining its commitment to education and health services for the people of its state, while building a steadily growing and diverse environment for medical research. The School of Medicine remains the University’s largest source of contract and grant funding, with faculty bringing in $431 million in 2014. The School of Medicine houses the Center for Genomics and Society and the Department of Social Medicine, which will play key roles in this K99/R00.

Center for Genomics and Society

The training component of this K99/R00 will be based in the UNC Center for Genomics and Society (CGS), an NIH P50-funded “Center of Excellence in ELSI Research” housed within the Department of Social Medicine at UNC’s School of Medicine. Two of the three mentors on this grant are active participants at CGS, which is now entering its seventh year of funding and is supported until 2018. Dr. Henderson is the Director of the CGS and Dr. Debra Skinner is the Associate Director and Training Director. CGS provides a rich learning and research environment for trainees because it brings together investigators from numerous fields such as medical genetics, genetic counseling, bioethics, sociology, anthropology, law, public health, philosophy, and nursing. CGS’s goal is to carry out an integrated set of transdisciplinary research, training, and policy activities addressing ethical, legal and social issues involved in the application of genomics to the general public. To create a real-world context in which to study this application of genomics, CGS investigators are designing and conducting a trial protocol informed by ELSI perspectives, recruiting 1,000 individuals within a controlled setting, focusing on highly penetrant rare mutations that place people at risk for potentially preventable conditions.

Department of Social Medicine

The Department of Social Medicine, chaired by Dr. Gail E. Henderson, is an academic unit that incorporates the long-standing interest of the University of North Carolina and the School of Medicine in community medicine and health care delivery systems. The mission of the Department is to inform the work and thought of physicians on: 1) the social conditions and characteristics of patients, the social causes of illness and the social barriers to effective care; and 2) the social responsibilities of the medical profession. Members of the faculty apply their various disciplines to problems of the poor, elderly, chronically ill, and other categories of people with special health and medical care needs; questions of allocation, distribution, organization and financing of health resources; and health and medical care problems in North Carolina.

The Department carries out its mission through a variety of educational, research, and service activities in several venues and almost always in interdisciplinary collaboration throughout the UNC campus. Though not an exclusive list, the following areas are those in which the Department has active research and ongoing

interests: cultural anthropology and medical anthropology, epidemiology, health economics, history of medicine and public health, literature and medicine, medical care organization, medical ethics, medical sociology, medicine and the law, preventive medicine, public policy in health and medical care.

The Department of Social Medicine, unlike other departments in the University, serves as an interdisciplinary department, and employs faculty and researchers from across the campus and beyond to accomplish its mission. This means that the administrative staff in the department is exceptional in terms of their ability to comprehend and coordinate activities across the wide array of constituencies served by the department. Social Medicine is a bridge between medicine and public health, and between medicine and the arts and humanities disciplines, and those who work in Social Medicine must have strong skills in translation and organization.

Center for Bioethics

The UNC Center for Bioethics will be a valuable resource for the training components of this K99/R00, particularly training in the responsible conduct of research. Larry Churchill, Ph.D. and Laura Hanson, M.D. originally proposed the UNC Center for Bioethics as the “Center for Health Ethics and Policy” in 1999. They served as its founding Co-Directors when the University established it as a unit of the School of Medicine in 2001. The mission of the UNC Center for Bioethics is to provide a core facility for collaborative capacity-building in bioethics at UNC. Today, the work at the Center for Bioethics is supported by funding from: UNC School of Medicine Dean’s Office, UNC Department of Social Medicine, UNC Health System, North Carolina Translational and Clinical Sciences Institute (NC TraCS), NC Center for AIDS Research, the Center for Genomics and Society at UNC, Fogarty International Center, National Institutes for Health, National Human Genome Research Institute, and the Doris Duke Foundation. The Center for Bioethics coordinates Research Ethics Grand Rounds, a monthly seminar on the ethical issues in the design and conduct of biomedical research involving human subjects, and houses UNC’s Research Ethics Consultation Service.

Department of Genetics

The Department of Genetics, chaired by Dr. Terry Magnuson, provides basic and applied genetic/genomic research, education and training at the interface between biology, chemistry, physics, computer science, mathematics, the social sciences, public health and medicine in order to have a profound effect on how medicine will be practiced in the future. The Department includes a clinical arm focused on medical genetics, which covers the broad spectrum of clinical genetic research from disease prevention to diagnosis and treatment. The Department is home to a distinguished group of genomics investigators, which includes Dr. James P. Evans, who will serve as a member of the advisory committee on this grant. The Department of Genetics also leads the Genomic Medicine Colloquium, a monthly peer group for post-doctoral or clinical trainees, whose work relates to any aspect of Genomic Medicine including basic discovery science, translational research, clinical/laboratory medicine, or ELSI research, to present works in progress. I am currently a member of this group and will continue with this opportunity as part of my K99 training.

School of Law

Established in 1845, the UNC School of Law is among the oldest law schools in the nation and has played influential roles in the state, the south, and throughout the nation. UNC Law faculty includes world-class scholars, award-winning teachers, and noted practitioners. An impressive new series of externship and clinical programs—combining academic rigor with essential professional practice—has invigorated the second- and third-year learning experience. Rigorous joint degree programs in business, public policy, planning, social work and public administration assure diverse methods of inquiry. Forty-seven full-time professors conduct classes in a range of specialties. Many of the faculty come to UNC Law from public and private practice; others have combined the study of law with such disciplines as computer science, anthropology, history, theology, psychiatry, and philosophy. Over the past year, I have collaborated with UNC law faculty such as Dr. Conley, a CGS investigator, and health law professors Profs. Krause and Saver. Research conducted within the School of Law produces a rich body of publications - books, monographs, manuals, and articles in law reviews and other professional publications. Faculty members also participate in various local, regional, and national programs on continuing legal education sponsored by the School of Law and other organizations.

Gillings School of Global Public Health

The Gillings School of Global Public Health (SPH) at UNC was established in 1940 as the fourth school of public health in the US and the first to be created at a state university. The SPH at UNC is ranked first among schools of public health at public universities by *U.S. News & World Report* (last ranked in 2011), and second

among all schools of public health. The departments within the SPH include: Biostatistics; Environmental Science and Engineering; Epidemiology; Health Behavior; Health Policy and Management; Maternal and Child Health; and Nutrition. SPH faculty members such as Drs. Christine Rini and Dan E. Jonas are extensively involved in collaborative research with CGS and will also serve as useful resources for this K99/R00.

Frank Porter Graham Child Development Institute (FPG)

FPG was founded in 1966 by a small group of scientists who had a vision to conduct research that would make a difference in children's lives, support families, and inform public policy. Today FPG is one of the nation's oldest and largest multidisciplinary centers devoted to the study of young children and their families. FPG has a long history of obtaining federal funding to conduct training and research projects to address the health and education of young children. With approximately 280 employees, research and training projects are conducted by an interdisciplinary faculty with backgrounds in anthropology, education, maternal and child health, pediatrics, nursing, psychology, social work, speech and hearing sciences, and related fields. Research projects focus on genetic disorders; developmental disabilities; early care and education; physical and social health; professional development, technical assistance, and implementation science; public policy and evaluation; and racial, ethnic, linguistic, cultural, and socioeconomic diversity. Core units within FPG offer support for the successful implementation of grants. These include the Publications Office, the Data Management and Analysis Center, and Qualitative/Ethnographic Methods & Analysis Core (QMAC). QMAC, directed by Dr. Skinner**,** Co-Mentor on this K99/R00, will be a particularly useful resource for the qualitative research planned in this proposal. It will provide an experienced staff and resources to assist in all aspects of qualitative/ethnographic research, including research design, training, implementation, data management, collection, and analysis.

In addition to the above UNC Departments that house CGS investigators and resources that can be utilized to support the work of the grant, I will also audit classes within the following three departments.

School of Education

Founded in 1885, the School of Education was one of the first professional schools established at the University of North Carolina at Chapel Hill. Its mission is to support students, educators, schools and families in the state of North Carolina and across the nation through innovative instructional programs, scholarship and partnerships. The School’s goal is to help ensure that every student has the opportunities and support needed to reach her or his maximum potential as an individual, worker, family and community member and citizen of a democratic society. The School ranks in the top 15 percent of schools of education nationwide. In March 2014, U.S. News & World Report ranked the School of Education 36th among the public and private schools of education across the United States that were included in the ranking.

Department of Sociology

Founded in 1920 by Howard W. Odum, the Department of Sociology has played a prominent role in the development of sociology as a major field of study in the social sciences. Judged “distinguished” in the 1930s by an American Council of Education evaluation, it continues to be regarded as one of the very best in the world. The department’s houses a variety of institutes, centers and interdisciplinary programs including: The Odum Institute for Research in Social Science; the Carolina Population Center; and the Kenan Institute for the Study of Private Enterprise.

Department of Statistics and Operations Research

The Department of Statistics and Operations Research specializes in inference, decision-making, and data analysis involving complex models and systems exhibiting both deterministic and random behavior. It focuses on developing and analyzing the necessary quantitative and computational tools to enable practitioners to solve problems in statistical and probabilistic analysis, modeling, optimization, and the evaluation of system performance. Its faculty engage in fundamental research in probability, statistics, stochastic processes, and optimization, and are also heavily involved with interdisciplinary areas of application such as genomics, biological modeling, environmental statistics, insurance and financial mathematics, revenue, workforce, and supply-chain management, traffic flow and congestion, and telecommunications.

Finally, I will utilize the following resources for trainings and research assistance for both Aim 1 and 2 of this proposal.

Odum Institute for Research in Social Science

The Odum Institute will also be an important resource for this K99/R00 because it provides training in empirical social science research methods and qualitative data analysis. The Odum Institute houses one of the nation's largest social science and census data archives, maintains a state-of-the-art Geographic Information System (GIS) and computing lab. It also provides advanced statistical software and consulting support for social science and survey research design and analysis, offers short courses and seminars on research and related topics, and sponsors 16 ongoing faculty work groups.

The Institute's services are available to faculty and graduate students, undergraduate students and faculty mentors, academic departments, UNC centers and institutes, university staff and administrators, other research groups and partners, government officials and the public. The Institute is staffed by experts in quantitative and qualitative research methods, statistics, survey research, and social science and census data archives. Its short course faculty draws from leading national and international experts throughout the Triangle's research community. The Institute supports multidisciplinary social science research in a variety of ways. The Institute's Survey Research Group supports the university's only Certificate Program in Survey Methodology for social scientists and graduate students. In addition to the Institute's upgraded survey research capability, the Survey Research Group offers consultation and services on questionnaire design and pre-testing, data collection (including surveys), sample design, data analysis, and focus group research.

The North Carolina Translational and Clinical Sciences Institute (TraCS)

TraCS offers a variety of resources for researchers at UNC that I will utilize during this K99/R00 grant. TraCS houses training for K-awardees in the responsible conduct of research and offers training in mentorship that will be an integral part of my training plan. TraCS is the integrated home of the Clinical and Translational Science Awards (CTSA) program. The aims of TraCS are to: 1) Expand to support the full spectrum of clinical and translational research; 2) Focus on three strategic initiatives: next-generation technologies to transform clinical research and practice, new paradigms and resources to accelerate drug development, and comparative-effectiveness research to provide definitive evidence of the benefits and harms of tests and treatments; and 3) Train, support and motivate the next generation of clinical and translational researchers.

Office of Postdoctoral Affairs

The Office of Postdoctoral Affairs (OPA) at UNC offers a wide variety of trainings and professional development trainings for postdoctoral fellows at the university. Its mission is to enhance, support, and promote postdoctoral training at UNC and help to prepare postdoctoral scholars for successful research careers. OPA serves postdoctoral scholars, faculty, and human resources professionals in all disciplines, schools, and colleges across the University. The goals of OPA are to: 1) advocate for postdoctoral scholars and the greater postdoctoral scholar community; 2) educate postdoctoral scholars and the campus community about University policies, postdoctoral rights, and other concerns related to postdoctoral scholars; 3) build effective career management skills and develop the professional skills postdoctoral scholars need both in and outside the lab; 4) support faculty mentors in the recruitment, mentoring, and professional development of productive postdoctoral scholars; and 5) collaborate with campus services to address the issues, concerns, and needs that are unique to the postdoctoral scholar population. OPA also offers one-on-one career counseling support to assist with job searches, applications, and job talk preparation.

Library Resources

The UNC Library system comprises nearly three dozen libraries, including the Walter Royal Davis Library, which is the main Academic Affairs library, the House Undergraduate Library, the Katherine R. Everett Law Library, and the Health Sciences Library, which is the main Health Affairs library. Campus libraries have more than three hundred staff, and the library's combined holdings exceed 5,000,000 volumes, 4,000,000 microforms, 2,000,000 printed government publications, 16,000,000 manuscripts, hundreds of thousands of audiovisuals, maps and photographs, and thousands of electronic titles. In scope, campus libraries cover most areas of the fine arts, biomedical and physical sciences, humanities, law, and social sciences. The library offers research support with librarians who specialize in the research area of interest.

The UNC Health Sciences Library (HSL)

The HSL, part of the UNC Library system, has superb staff, facilities, and collections and is considered to be among the best medical school libraries in the United States and Canada. The six-story building has seating capacity for 713 users. The HSL has over 328,000 volumes, and 3,950 journals (about 3,000 of these are also available electronically). The HSL and the School of Medicine's Office of Information Services jointly support the University of North Carolina Literature Exchange (UNCLE), a locally mounted, networked version of MEDLINE, the major bibliographic database in the biomedical sciences and clinical medicine. This Web-based system is available free of charge to all members of the University health affairs community and is easily accessible from any location on or off campus. In addition, HSL has an online system that provides information about material available at the other area institutions of higher learning. Information about other resources and databases can be obtained at the library's Internet Desk, which is staffed on a full-time basis by technical experts. The HSL is also a participant in faculty and student education related to the retrieval of electronic information and use of specialized computer applications.

The Katherine R. Everett Law Library

The Katherine R. Everett Law Library houses a rich collection of law and law-related materials to support the research and teaching of the UNC Law School community, and the larger University of North Carolina-Chapel Hill community. The Law Library print collection contains materials in the following categories: United States federal and state law collections; foreign and international collections; government publications; and special collections and rare books. The Law Library will be a particularly helpful resource for this K99/R00 proposal because it strives to collect international law at the research level. The collection includes treaties, international legal periodicals, international treatises, and other monographs. Foreign law, published in English, is collected at the Law Library at an instructional support level as required by the teaching at the University of North Carolina School of Law. This collection includes a number of foreign legal periodicals. There has been an emphasis in the past on collecting legal materials from common law countries, particularly Canada.

Equipment

No item of property that has an acquisition cost of $5,000 or more will be necessary for this project.

Foreign Justification

This grant proposal seeks to provide guidance for US policy regarding how life, long-term care, and disability insurers are, or should be, legally allowed to use genetic information in underwriting decisions such as setting premium rates or accepting insurance applications. The project specifically focuses upon how actuarial justification standards apply to genetic information. Actuarial justification policies generally require insurers to demonstrate statistical correlation between a risk and an increased likelihood of cost to the insurer. The US has no federal laws regarding supplemental insurer use of genetic information. Eight states have actuarial justification laws specific to genetic information and life insurers, and all fifty states have some form of broader actuarial justification laws applicable to at least one type of supplemental insurance that apply to medical information overall. However, these laws do not explicitly define actuarial justification as it relates to genetic information nor delineate the necessary levels of statistical evidence that insurers must show in order to meet actuarial standards. Determining statistical correlation in this area is not a straightforward endeavor given the varying predictive values of genetic variants and the varying preventive measures one can sometimes take to lower genetic risk. Currently US law does not provide guidance as to how actuarial standards should be interpreted or enforced in the context of the predictive value or preventive measures.

Although US law does not provide clear guidance on actuarial justification standards, the international community affords an opportunity to gain insight into how actuarial standards can be used in the context of genetic information. A recent review of international policies found 45 countries with policies regarding insurer use of genetic information (Atkinson 2009) and several of these countries have had actuarial policies specific to genetic testing and supplemental insurers in place since the early 2000's (ALRC 2003, HMG 2011). These policies often apply to supplemental insurance that is generally privatized, similar to the US supplemental insurance market. Furthermore, the majority of the academic and policy discussions in this area have occurred abroad. For example, of the 77 books and journal articles referenced in this grant proposal, in 37 the primary author is an international scholar. Given the long-standing policies of many countries in this area, the international context provides a critical opportunity for research with the goals of understanding the background for, implications of, and lessons from the policy mechanisms utilized globally. These data will then inform a nuanced view of US policy options. Thus, Aim 1 of this proposal undertakes case studies of four countries: one pilot study and one additional case study for each of the three predominate policy mechanisms utilized in this area (moratorium, legislation, and guideline).

After an initial consultation with qualitative and quantitative methodologists at the UNC Odum Institute for Research in Social Science and discussions with my mentors, it became clear that to gather the nuanced case study data that I am seeking, in-person document collection and interviews are necessary. I am proposing travel to four countries to conduct these studies for two primary reasons.

First, one of the two forms of data that I will analyze for the case studies are policy documents. While some documents, especially the official legislation or guidelines of the government, will be available online, I propose to gather a broad range of policy documents such as government reports or legislation, legislative history, internal government or insurance communications, legal case documents, and academic critiques or manuscripts regarding the policies. Travel to the country will allow me to meet with a research librarian familiar with the specific international context and to collect primary source documents unavailable within the US.

Second, conducting the in-depth key informant interviews in person will help ensure the quality of the interview data and will likely increase the number of individuals willing to be participants. I considered options of telephone and video interviews, but felt that disadvantages of these options outweighed the advantages. Telephone interviewing could lead to a loss of many of the nuances and non-verbal analysis available in person (King 2010). Additionally, being physically present in the country will allow me to more effectively build rapport and to conduct interviews with additional stakeholders within the interviewee's professional environment. Video interviews using technologies such as Skype are possible, but video interviewing has been cautioned against due to the unreliability of the technology, the difficulty of recording interviews through these mediums, and the necessity of proper equipment for both interviewers and interviewees (King 2010, Guest 2012).

In my budget, I calculated travel costs at 75% of the maximum daily per diem rates according to the US State Department for 12 days in each country, thus allowing for ample time to conduct document searches and interviews. No foreign individuals will receive compensation or funding from research funds.

Budget Justification

Year 1 and 2 Personnel

Personnel:

Principal Investigator: Anya Prince, JD, MPP, currently Post-Doctoral Research Fellow at the University of North Carolina Center for Genomics and Society (CGS), will be the Principal Investigator (PI) on this proposal (EFFORT in mentored years 1 and 2). During Years 1 and 2 she will undergo training in qualitative and quantitative data collection methods and research design and will conduct case study analysis of international countries with actuarial justification policies and survey US state insurance commissioners on enforcement of actuarial justification and unfair trade practice laws. As part of her training, Ms. Prince will attend courses and seminars on topics including case study methods, interview methods, and survey design.

Benefits: Benefit support is requested for the PI at the University rate of 8.968%, plus $3685.20 per year for health insurance.

Research Assistance - Institutional Base Salary Every summer, CGS hires a law student as a research assistant to aid in the legal projects of the Center. He or she works for 12 weeks in May-July at a rate of Institutional Base Salary Ms. Prince will contribute to the cost of this research assistant so that the student will work on her project for 20% of their time at CGS. This student will not only provide Ms. Prince with valuable research support, but will also provide her with the opportunity to work on the mentoring skills as specified in the training plan, while still under the guidance of Ms. Prince's mentors. In Year 1 this student will assist with the collection of legal and policy documents for the case studies, as well as analysis of the pilot case study (8 hours per week for 12 weeks at Institutional Base Salary + 110 SS).

Year 1 Research Costs

Supplies - $2225: Ms. Prince will purchase a laptop computer for $1425. Additionally, reference software, such as Endnote, and text analysis software, such as NVivo 10 or Atlas.ti, will be purchased for an additional $500. This computer and software will be exclusively used for the training and research tasks of the proposal, including qualitative, quantitative, and legal analysis. Ms. Prince will also purchase a digital tape recorder ($300) to be used for the in-depth key informant interviews.

Travel

AALS Conference - $2200: In January 2016, Ms. Prince will attend the American Association of Law Schools (AALS) Conference in New York, New York. At this conference, Ms. Prince will attend a workshop on qualitative and mixed methods [airfare - $300, hotel - $1000 (250 X 4 nights), meals - $200 (40 X 5 days), registration - $600, incidentals - $100 (shuttle, taxi, or parking to/from airport at home and destination)].

Case Study 1 (Pilot case in Canada) - $3232: As part of Aim 1, Ms. Prince will conduct a pilot case study in Canada. During her trip spanning twelve days (ten business days), Ms. Prince will collect policy documents from research and government libraries and conduct in-depth interviews with key stakeholders. For the Canada case study Ms. Prince will spend approximately six days in Ottawa and six days in Montreal. As the capital of Canada, Ottawa is an important destination to interview policy experts and government officials. Montreal, only two hours away from Ottawa, is the location of Ms. Prince's primary contact in Canada, Yann Joly at the University of McGill [airfare - $450, transport between Ottawa and Montreal - $149, Ottawa - $1265 [hotel - 810 (135 X 6), per diem - 455 (65 X 7)], Montreal - $1368 [hotel – 900 (150 X 6), per diem - 468 (78 X 6)]]. Hotel rates are based on 75% of the maximum daily rates for hotel in each city and per diem (including meals and incidentals, such as taxi and metro to interviews and travel to and from the airport) is 75% of the maximum daily rate from the US State Department (http://aoprals.state.gov/web920/per_diem.asp).

LSA Conference - $2040: In June 2016, in order to disseminate her initial research findings from Canada and her project methodology and to be informed of the latest research combining legal and empirical research methods, Ms. Prince will attend the Law and Society Association Annual Meeting in New Orleans, LA. Because it is cheaper to purchase both a membership to the society and register for the conference than to register as a non-member, Ms. Prince is requesting funding for both membership fees and conference registration [airfare -

$420, hotel - $920 (230 X 4 nights), meals - $200 (40 X 5 days), registration - $300, membership - $100, incidentals - $100 (shuttle, taxi, or parking to/from airport at home and destination)].

Case Study 2 (Non-European Union Country TBD) - $5234: In addition to the pilot case study in Canada, Ms. Prince will complete one additional case study to a non-European Union(EU) country in Year 1. Like the Canadian pilot study, this trip will span twelve days (ten business days) to provide ample time for interviews and document collection. Determination of which countries will be included in this case study will be made in Year 1 after initial research and discussion with key stakeholders and in light of lessons learned from the pilot case study. Examples of possible non-EU countries with policies in this area include Australia, Japan, Israel, and South Africa. Hotel and per diem rates are based on the average of rates in a sample of non-EU countries with policies from this area. Rates are 75% of the maximum daily rates from the US State Department. Per diem costs include meals and incidentals, such as taxi and metro to interviews and travel to and from the airport. Airfare is based on rates from Kayak searches [airfare - $1800, hotel - $2160 (180 X 12), per diem - $1274 (98 X 13)].

Other Expenses

Transcription - $2400: Transcription services are required for this project to transcribe the case study interviews. There will be an estimated 24 hours of audio recordings (24 X $100 per audio file hour for transcription).

Classes and Trainings - $1000: In order to gain sufficient training in qualitative and quantitative data collection and research methods, Ms. Prince will attend trainings through the Odum Institute for Social Science Research and audit UNC classes in empirical social science research methods. The Odum Institute short courses and training range from no cost to $200. The audit fee for UNC classes is $20 and Ms. Prince will audit four classes in the first year. Textbooks and class materials will vary depending on the class and the professor/syllabus for the course; however costs could run as high as $150 for some classes (audit - $80 (4 X 20), textbooks - $460, Odum classes - $540 (6-8 trainings)).

Printing/Copying Expenses - $100: In order to get copies of policy documents from libraries and stakeholders for the case studies, Ms. Prince will need to print or copy documents that are not available online. She will use up to $100 in printing and copying expenses ($50 for each case study x 2 studies in Year 1).

Westlaw Access - $3969: WestlawNext will be purchased for research access to law reviews and federal and state case law, statutes, and regulation. This is a necessary resource for the kind of legal and public policy research and analysis that will be conducted in this project. Employees of the UNC School of Medicine do not have access to this legal database through the UNC library system; therefore, funds are required to offset the cost for access.

Odum Methods Support - $550: Throughout the project, Ms. Prince will confer with methodologists at the Odum Institute for support and suggestions related to the case studies and survey. This will occur during research planning, data collection, and analysis (10 hours X 55 per hour of support per year).

AALS Application fee: $500: Securing a tenure track position as an essential component of the R00 portion of this grant mechanism. Therefore, Ms. Prince will participate in the centralized recruitment system of the law school hiring market. Under this system, the American Association of Law Schools (AALS) collects applicant resumes in a central database sent to law schools across the country with open tenure track positions. Although Ms. Prince will also reach out to law schools directly, participation in this centralized application is an essential part of law school hiring.

Total Year 1 Research Costs: $25,000

Year 2 Research Costs

Supplies - $450: In Year 2 Ms. Prince will renew licenses for purchased software, such as Endnote, NVivo 10, or Atlas.ti, and will purchase a license for a quantitative data analysis program such as SAS or Stata (Endnote renewal - $100, NVivo renewal - $150, Stata license - $200)

Travel

In Year 2, Ms. Prince will complete the remaining proposed case studies in two EU countries. The majority of policy regarding the use of genetic information in supplemental insurance has occurred in Europe. Therefore,

two of the three total case studies will be selected in Europe. Airfare to these EU countries ranges from $1200-1600. These trips will span twelve days (ten business days) to provide ample time for interviews and document collection. Determination of which countries will be included in these case studies will be made in Year 1 after initial research and discussion with key stakeholders and in light of lessons learned from the pilot case study. Examples of possible EU countries with policies in this area include the UK, Norway, Ireland, Germany, and Portugal. Hotel and per diem rates are based on the average of rates in a sample of EU countries with policies from this area. Rates are 75% of the maximum daily rates from the US State Department. Per diem costs include meals and incidentals, such as taxi and metro to interviews and travel to and from the airport. Airfare based on rates from Kayak searches

Case Study 3 (EU Country TBD) - $5204: Case study 3 will examine the policies of an EU country regarding supplemental insurer use of genetic information [airfare - $1400, hotel - $2400 (200 X 12), per diem - $1404 (108 X 13)].

Case Study 4 (EU Country TBD) - $5204: Case study 4 will examine the policies of an EU country regarding supplemental insurer use of genetic information [airfare - $1400, hotel - $2400 (200 X 12), per diem - $1404 (108 X 13)].

ASBH Conference - $1940: To disseminate research findings, Ms. Prince will attend the October 2016 annual meeting of the American Society of Bioethics and Humanities in Washington, DC. This conference will also provide Ms. Prince with an opportunity to network with a wide variety of interdisciplinary scholars and to be informed of cutting edge bioethics research. Because it is cheaper to purchase both a membership to the society and register for the conference than to register as a non-member, Ms. Prince is requesting funding for both membership fees and conference registration [airfare - $300, hotel - $800 (200 X 4 nights), meals - $240 (40 X 6), registration - $400, membership - $100; incidentals - $100 (shuttle, taxi, or parking to/from airport at home and destination)].

LSA Conference - $2000: Additionally, in June 2017, in order to disseminate her research findings to the legal community and to be informed of the latest research combining legal and empirical research methods, Ms. Prince will attend the Law and Society Association Annual Meeting in a TBD location. Because it is cheaper to purchase both a membership to the society and register for the conference than to register as a non-member, Ms. Prince is requesting funding for both membership fees and conference registration [airfare, hotel, and meals - $1500, registration - $300, membership - $100, incidentals - $100 (shuttle, taxi, or parking to/from airport at home and destination)].

AALS Interview Sessions - $1108: As a continuation of the law school hiring process after the submission of the centralized AALS application in Year 1, Ms. Prince will attend the national AALS hiring conference where law schools from across the country conduct initial interviews with potential tenure-track professor candidates. This is an essential component of this training grant, since securing a tenure track position is a requirement of the R00 portion of the grant [airfare - $288, hotel - $600 (200 X 3 nights), meals $120 (40 X 3), incidentals - $100 (shuttle, taxi, or parking to/from airport at home and destination)].

Other Expenses

Transcription - $2400: Transcription services will continue in Year 2 for the second half of the case study interviews (24 X $100 per audio file hour for transcription).

Classes and Trainings - $425: In Year 2, Ms. Prince will continue her training in qualitative and quantitative data collection and research methods through the Odum Institute for Social Science Research and UNC classes. The Odum Institute short courses and training range from no cost to $200. The audit fee for UNC classes is $20 and Ms. Prince will audit one class in the second year. Textbooks and class materials will vary depending on the class and the professor/syllabus for the course; however costs could run as high as $150 for some classes (audit - $20, textbooks - $100, Odum classes - $305 (3-5 trainings)).

Printing/Copying Expenses - $100: In order to get copies of policy documents from libraries and stakeholders for the case studies, Ms. Prince will need to print or copy documents that are not available online. She will use up to $100 in printing and copying expenses ($50 for each case study x 2 studies in Year 2).

Survey Costs - $100: The insurance commissioner survey of Aim 2 will be designed by Ms. Prince with support from mentors and methodologists at the Odum Institute. Recruitment for the surveys will be primarily via email

and follow-up phone, although at least one official recruitment letter will be sent as follow-up for those offices that do not respond to initial requests. The survey will be primarily web-based and designed through Qualtrix. Given these methods, there is little cost associated with the survey other than a small sum ($100) for copying and mailing the follow up letters (via Fed-ex). Other design costs are included in the salary of Ms. Prince and support from the research assistant and Odum Institute, or are free online services available at UNC, such as email and Qualtrix.

Westlaw Access - $3969: Ms. Prince will continue to use WestlawNext to conduct legal and policy research.

Odum Methods Support - $550: Ms. Prince will continue to utilize Odum Institute research support as needed. Year 2 will focus on survey development support (10 hours X $55 per hour of support).

Total Year 2 Research Costs: $25,000

Indirect Costs: The indirect cost rate for Year 1 and 2 of the K99/R00 contract that begins 9/1/2015 and ends 8/31/2017 is 8%.

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix: Ms.
First Name*: Anya
Middle Name:
Last Name*: Prince
Suffix:

2. Human Subjects

Clinical Trial? ● No ○ Yes
Agency-Defined Phase III Clinical Trial?* ○ No ○ Yes

3. Permission Statement*

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

● Yes ○ No

4. Program Income*

Is program income anticipated during the periods for which the grant support is requested? ○ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount ($)*	Source(s)*

Funding Opportunity Number: PA-15-083. Received Date: 2015-02-11T15:56:35.000-05:00

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5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ● No ○ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ○ Yes ○ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ○ Yes ○ No

7. Change of Investigator / Change of Institution Questions

❑ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

❑ Change of Grantee Institution

Name of former institution*:

PHS 398 Career Development Award Supplemental Form

OMB Number: 0925-0001

Introduction (if applicable)	
1. Introduction to Application (for RESUBMISSION applications only)	
Candidate Information	
2. Candidate's Background	1251-2_Candidates_Background.pdf
3. Career Goals and Objectives	1252-3_Career_Goals_Objectives.pdf
4. Career Development/Training Activities During Award Period	1253-4_Candidates_Plan.pdf
5. Training in the Responsible Conduct of Research	1254-5_Responsible_Conduct_Research.pdf
6.Candidate's Plan to Provide Mentoring (as applicable)	
Statements of Support	
7. Plans and Statements of Mentor and Co-Mentor(s)	1255-7_Plans_and_Statements_Mentors.pdf
8. Letters of Support from Collaborators, Contributors, and Consultants	1256-8_Letters_of_Support.pdf
Environment and Institutional Commitment to Candidate	
9. Description of Institutional Environment	1257-9_Institutional_Environment.pdf
10. Institutional Commitment to Candidate's Research Career Development	1258-10_Institutional_Commitment_to_Candidate.pdf
Research Plan	
11. Specific Aims	1259-11_Specific_Aims.pdf
12. Research Strategy*	1260-12_Research_Strategy.pdf
13. Progress Report Publication List (for RENEWAL applications only)	
Human Subject Sections	
14. Protection of Human Subjects	1261-14_Human_Subjects_Protections.pdf
15. Inclusion of Women and Minorities	1262-15_Inclusion_of_Women_and_Minorities.pdf
16. Inclusion of Children	1263-16_Exclusion_of_Children.pdf
Other Research Plan Sections	
17. Vertebrate Animals	
18. Select Agent Research	
19. Consortium/Contractual Arrangements	
20. Resource Sharing Plan(s)	
Appendix (if applicable)	
21. Appendix	
Citizenship*:	
Personal Info	

Tracking Number: GRANT11832934

Funding Opportunity Number: PA-15-083. Received Date: 2015-02-11T15:56:35.000-05:00

Candidate's Background

In 2007, during a joint degree program in law and public policy at Georgetown University, I took an ethics class, "Contemporary Issues in Genetics and Society." This class stimulated my interest in the ethical, legal, and policy issues surrounding genetic testing and inspired me to pursue a career in genetics law and policy.

In law school I participated in a health policy clinic at the Harrison Institute for Public Law. There, I managed two projects for the Genetics and Public Policy Center. The first examined how state false advertising laws could be applied to direct-to-consumer marketing of genetic tests. The second performed an initial review of state laws addressing the use of genetic information in supplemental insurance. This review examined genetic-specific laws only, not state unfair trade practice laws or the specifics of actuarial requirements. This K99 grant builds upon my initial review, but delves much further into the issues. In graduate school I also gained training in statistical analysis through my public policy thesis on social disparities in the access and utilization of genetic testing. For this project I analyzed data from the National Health Interview Survey. I also completed an externship in the Bioethics Department at NIH. This externship culminated in a published paper in the *Journal of Law, Medicine & Ethics,* which explored how the law grapples with defining difficult medical concepts.

After graduate school I was awarded a Skadden Fellowship to work on genetic-related legal issues. Described as "a legal Peace Corps," the Skadden Fellowship Foundation provides two-year, fully funded stipends for promising law graduates to design a public interest project in a non-profit organization. I chose to create a project at the Cancer Legal Resource Center (CLRC), an organization that provides free legal resources to individuals with cancer. In this position I assisted individuals with genetic predispositions to cancer with their legal concerns about discrimination and access to preventive care. Through this fellowship I became one of the only attorneys in the US providing free legal services to those experiencing genetic discrimination. I have seen firsthand how laws, such as GINA, operate on the ground. I was able to assist clients through successful appeals of life and disability insurance denials based on genetic information. I supervised clinical law students as they answered the legal questions of individuals with cancer and genetic predispositions to cancer. Finally, I guest lectured at several universities and spoke at advocacy and professional conferences on genetic discrimination, insurance coverage of preventive interventions, and employment and insurance law.

In 2012, based on my legal expertise in GINA, I was invited to join a collaboration of academics across the international community exploring genetic policy issues. Michael Waterstone, Associate Dean at Loyola Law School, and I co-authored a chapter on GINA for *Genetic Discrimination: Transatlantic Perspectives on the Case for a European Level Legal Response*, edited by my advisory committee member, Dr. Aisling De Paor. This experience provided me valuable lessons about how privacy and insurance access concerns of individuals and policy experiences of countries across the world have many similarities. This project also offered insight into how an academic research career could afford me an opportunity to explore the broader legal and policy implications of issues I assisted my clients with on a day-to-day basis. While I enjoyed the direct legal advocacy and outreach of the CLRC, I began to consider a research career. In 2013, to explore this option, I completed a law review analyzing the necessary elements of state law to provide individuals with comprehensive protection from misuse of genetic information. Although this paper briefly touched upon state actuarial laws, it did not include a comprehensive analysis on the topic.

These endeavors solidified my interest in a research career and, in 2014, I began a position as a Postdoctoral Research Fellow with the Center for Genomics and Society (CGS) at UNC-Chapel Hill (P50HG004488). My time at CGS has provided me with unparalleled opportunity to explore ELSI issues, particularly surrounding genomic testing of asymptomatic adults. In my first year, I have published five articles, including a commentary in *Genetics in Medicine*, and two that focus on GINA and the gaps in GINA. My prior experiences and my present position have reinforced my commitment to a career in ELSI legal research.

While this background has laid the groundwork for me to become a successful investigator, it is clear that I need to strengthen my skills in qualitative and quantitative data collection and analysis to become a well-rounded, independent researcher. I have strong training in legal, policy, and basic quantitative analysis, but not in the skills to collect social science and empirical data central to my research interests, and importantly, am currently unable to design a research inquiry from start to finish. Building these skills will enable me to design and conduct multiple methods projects that can answer important questions regarding the legal and policy implications of genomic technologies. I believe that the K99 period of this grant will provide me with opportunities to fill the gaps in my training to make me a fully competent and independent transdisciplinary researcher.

Career Goals and Objectives

Current and future research

My scholarly research examines the growing landscape of laws protecting individual genetic rights and policies providing insurance access to genetic testing and follow-up services. To date my work has analyzed how GINA has played out at the ground level with a focus on the gaps in GINA and state efforts to fill these gaps. My past work at the CLRC has focused my attention on the perspective of individuals, patients, genetic counselors, and families. Through this lens I aim to suggest practical solutions to gaps in the laws.

Currently, as a member of the CGS research team, I have actively participated in the implementation of the Center's research project: "GeneScreen." GeneScreen investigates the ethical, legal, and social implications of genomic screening for a targeted panel of medically actionable genetic variants in a healthy adult population. My first research activity at CGS examined insurance for the medically recommended follow-up interventions indicated by predictive genetic tests for preventive, adult-onset conditions. Access to insurance coverage and healthcare will remain a focus of my research both at CGS and throughout my career. Equitable access must be an ongoing consideration as the effects of healthcare reform become known and future policy changes are implemented to address shifts in medical knowledge.

My research has also focused on individual fear and experiences of genetic discrimination and the laws that attempt to address these concerns. For example, I co-authored a paper with Myra Roche, a genetic counselor and CGS investigator, titled "Genetic information, non-discrimination, and privacy protections in genetic counseling practice." This article provided case studies that may be encountered in genetic counseling and offered practical examples and options for counselors and their patients to understand the law and use legal protections to their advantage. I also wrote a peer response regarding employer medical certification requests and GINA in the *American Journal of Bioethics*.

This K99/R00 proposal is a natural extension of my past experiences and my research interests. Much of my scholarship in the area of state legislation regarding supplemental insurances has been broad surveys of what the laws cover and explanations of the gaps in coverage. This grant would provide me the opportunity to delve much deeper into one aspect of state law that is currently under-researched—actuarial justification. My research and professional background provides me a solid baseline understanding of the complexity of law and policy in this area, and the K99 portion of the grant will help me to acquire the requisite empirical research skills to collect and analyze the necessary data to investigate this important issue.

In my future scholarship, I will continue to examine the ways in which laws regarding genetic discrimination and use of genetic information play out in practice. However, with the benefit of additional K99 training, these interrogations will profit from robust analysis using multiple methods, both empirical and legal. I am interested in how laws and practices shape and are shaped within the legal realms of employment, insurance, medical records, and privacy. I am committed to exploring how policy changes and new ways of enforcing or interpreting laws can positively affect the rights and lives of individuals.

Career Objectives

My long-term career objective is to become an independent ELSI researcher who is able to design and implement rigorous legal and policy critique and analysis, collect empirical social science data, and design broad transdisciplinary examinations of laws and policies that directly affect individual rights and interests. Additionally, I have always been passionate about teaching and mentoring future legal scholars, and thus, my goal is to become a tenured law professor. In this role I would research ELSI issues and seek to teach an experiential course in which students would receive legal and policy training and help conduct research on the legal issues and concerns identified during my K99 grant projects. In August 2014, the American Bar Association (ABA) altered its accreditation guidelines to require all law students to complete an experiential learning course prior to graduation, a requirement that could be satisfied by students assisting with the research aims of this proposal in a structured class environment. In fact, using an experiential course model increases the chances of my success in securing a tenure track position, either as a teaching or clinical professor, at a law school for the R-phase. (See Waterstone Letter) While my goal is to teach this course during the R-phase of the grant, the grant funding would only be used to pay for my research and salary, and for items directly necessary to support the students in the research they undertake for this project. By teaching an experiential course, I could potentially magnify the outcomes of the research by building student research assistance into my project and, just as I was inspired during my law school years, provide a venue through which I can train future ELSI legal scholars.

Candidate's Plan for Career Development/Training Activities During Award Period

There are three primary goals for the K99 mentored phase of this project: To obtain 1) formal training in qualitative case study methodology and analysis; 2) formal training in survey design; and 3) professional development training in mentoring and supervising research assistants.

In my current position as Postdoctoral Research Fellow at CGS, I have researched ethical, legal, and policy implications of genomic sequencing in an asymptomatic adult population. Specifically, I have 1) honed my legal and policy research skills through production of a paper on insurance coverage of predictive genetic tests and interventions that help to lower risk of these diseases; 2) enhanced my ethical and legal research analysis skills by writing a paper about whether genomic researchers have an ethical, legal, or professional duty to place participant results in clinical medical records; and 3) learned how to conduct systematic evidence reviews through participation in a project to collect evidence of the harms and benefits of genomic screening for Lynch Syndrome among an asymptomatic population. Additionally, I have participated in the robust trainee program of CGS, led by Dr. Debra Skinner. Through this program, CGS trainees participate in three monthly activities: an ELSI-oriented journal club, a peer writing group, and a professional development seminar. I have also taken advantage of various UNC training programs including auditing Molecular Biology and Genetics, attending clinical and research ethics monthly grand rounds, participating as an intern on the Hospital Ethics Committee, and taking a refresher course on utilizing Stata for quantitative analysis at UNC's Odum Institute.

My interdisciplinary and collaborative experience at CGS has been invaluable. However, I believe I would greatly benefit from the targeted training plan outlined for the K99 mentored phase. As a member of the GeneScreen project team, I have gained exposure to the process of implementing a study design. It is clear that a strong background in qualitative and quantitative methods is needed to be able to design and implement a transdisciplinary research study. In concert with advice from my mentors, I decided that a K99/R00 grant would provide the additional empirical training I need to prepare for a career as an independent researcher.

Team*:* My **K99 co-mentors** will provide support, training, and advice. I will meet weekly with my primary mentor and at least monthly with my co-mentors. We will also talk as needed about specific research questions and trainings. The entire mentoring team will meet quarterly. (See Mentor Statements and Biosketches)

Gail Henderson, PhD: Dr. Henderson will be my primary mentor for the K99 phase of the grant. Currently, she is my primary mentor, so we have an established and strong mentor/mentee relationship. Dr. Henderson is a sociologist with over fourteen years of experience researching ELSI issues in genomic technologies. She has developed and implemented both quantitative and qualitative research projects. She is Principal Investigator of CGS and Chair of the Department of Social Medicine. In her role as my primary mentor, Dr. Henderson will provide support and training on qualitative and quantitative methods, as well as professional development.

Debra Skinner, PhD: Dr. Skinner is a sociocultural anthropologist with an extensive research background in mixed methods and qualitative studies of how families of children with disabilities and adult patients understand and use genetic information, as well as ethnographic studies of the production of genomic medicine. Additionally, she has been the Associate Director and Training Coordinator of CGS for 7 years. She is a Senior Scientist and Director of the Qualitative/Ethnographic Methods and Analysis Core at UNC's FPG Child Development Institute. As a co-mentor, Dr. Skinner will assist with training on qualitative methods as well as professional development training in supervision and mentorship.

Mark Hall, JD: Professor Hall is a leading scholar in insurance law, public policy, and bioethics. His scholarship has addressed the crossroads of ethics, insurance policy, and genetics for over fifteen years. Specifically, Prof. Hall has done case studies investigating health insurer use of genetic information through legal and policy analysis and interviews with state insurance commissioners. In his role as mentor, Prof. Hall will provide support and feedback on case study methods, and legal and policy analysis. Prof. Hall is a Professor in both the School of Medicine and School of Law at Wake Forest University, approximately two hours from UNC in Chapel Hill. Our monthly meetings will primarily be by phone, but we can also meet in person at least quarterly.

Additionally, my **advisory committee** will provide further support and guidance as questions arise in their fields of expertise. (See Letters of Support)

Angus Macdonald, PhD - Director of the Genetics and Insurance Research Centre (GIRC), Department of Actuarial Mathematics and Statistics, Heriot-Watt University: Dr. Macdonald is an Actuary and Professor in Edinburgh, Scotland. Since 1999, the GIRC has developed mathematical and actuarial models that incorporate genetic data and knowledge in order to explore the cost effects for insurers and individuals.

James Evans, MD, PhD – Professor of Genetics and Medicine, UNC: Dr. Evans is a nationally recognized clinical geneticist and researcher whose areas of focus include use of genomic technologies for gene discovery and clinical diagnosis and the policy implications of such technologies.

Mark Rothstein, JD – Director, Institute for Bioethics, Health Policy and Law, Univ. of Louisville: Prof. Rothstein has completed extensive legal, ethical, and policy research on bioethics, genetics, and insurance, including editing a book and authoring several articles on the use of genetic information in life insurance underwriting.

Aisling De Paor, BCL, LLM, PhD – Lecturer, Dublin City University, Ireland: Dr. De Paor is a Solicitor and Lecturer. Her research explores European genetic discrimination policies. She has published articles and a book on law and policy in this area, and on comparative analysis of other countries' policy responses.

Laura Koontz, PhD – Director of Policy, Ovarian Cancer National Alliance: Formerly, Dr. Koontz held the Genetics and Public Policy Fellowship sponsored by the American Society of Human Genetics and NHGRI. In this role she worked for Congresswoman Louise Slaughter exploring policy options for federal legislation regarding supplemental insurer use of genetic information.

Training Goals

Goal 1: To obtain formal training in qualitative case study methods and analysis: The application of actuarial justification and unfair trade practice laws to genomic sequencing is understudied in the US. There are limited qualitative, quantitative, and policy data available for analysis, all of which are needed to fully assess the policy implications of legislative and regulatory options. My proposed case studies will synthesize analysis from two data sources: international policy documents and semi-structured interviews. Thus, a primary component of my case study methods training will include instruction on interview methodology and qualitative data collection. This training will be beneficial as I develop subsequent research studies after completion of the K99/R00.

To gain skills in case study and interview methodology I will undertake four activities. First, I will attend the Qualitative Research Summer Intensive jointly sponsored by UNC's Odum Institute for Research in Social Science and ResearchTalk. This weeklong training offers courses on collecting, analyzing, and disseminating qualitative data, including trainings on interview methodology. I plan to attend this training in July 2015, prior to the start of the K99/R00 grant period. Funding for this training will be provided by CGS (See Henderson Letter). Second, I will audit the class, Case Study Methods, offered through the Department of Education. This class will provide a strong base knowledge of case study methods and analysis. Third, I will attend the American Association of Law Schools annual conference workshop on qualitative methods. This training will be uniquely beneficial because it focuses on the intersection between qualitative methods and legal research. Finally, I will attend additional trainings, as needed, on interview methods, qualitative analysis, and qualitative software programs through Odum Institute short courses. During the training period I will continue to shadow and work with Drs. Henderson and Skinner to implement and design the interviews in the GeneScreen project. I will put these acquired skills into practice in Aim 1 of the project in which I will conduct case studies of how international governments have addressed actuarial justification and genetic testing in supplemental insurance. Under the mentorship of Dr. Henderson, Dr. Skinner, and Prof. Hall, I will develop, conduct, and analyze interviews and undertake policy analysis as part of the international case studies.

Goal 2: To receive formal training in survey design: To gain skills in survey design I will undertake three activities. First, I will take two semester-long courses through the Odum Institute: Data Collection Methods in Survey Research and Questionnaire Design. Second, I will take additional short courses offered by the Odum Institute on survey methodology as needed during the training period. During my public policy degree training, I took two semester-long statistics classes and completed a thesis that utilized regression analysis of survey data. Given this background in quantitative analysis, my K99 training will focus specifically on survey design and data collection methods. If at some point during my research I find that I need to refresh my quantitative analysis skills, the Odum Institute offers short course trainings on quantitative analysis, such as the Stata training I took last year. Third, I will shadow Dr. Henderson and other CGS investigators in their work on survey design and analysis for GeneScreen. Under the mentorship of Dr. Henderson and Prof. Hall, I will design a survey of state insurance commissioners for Aim 2a in order to gather data on how actuarial justification and unfair trade practice laws are being interpreted and enforced in the context of genetic information.

Goal 3: To receive professional development training in mentoring and supervising research assistants: My career goal for the R00 phase of the grant is to lead students in legal and policy research in an experiential

learning course. In this capacity, the law students will essentially be research assistants as they help to conduct the legal and policy research of Aims 2b and 3. As such, leadership, mentorship, and supervision will be major components of the R00 portion of the grant. To prepare for this task, I will attend the 6-week course on mentorship conducted by the NC TraCS Institute, UNC's Clinical and Translational Sciences Award (CTSA). Drs. Skinner and Henderson will provide additional training and advice on mentorship and strategies for supervising student research. Additionally, every summer, CGS funds a law student research assistant to help with the legal projects of the Center. Through my K99 funding, I will pay a portion of this student's stipend so that he or she can assist with the aims of my project. This will not only provide important research support, but also provide me an opportunity to supervise a student while still in the mentored phase of my project.

Additional trainings: In the K99 phase of the project, I will continue to participate in CGS trainee activities, such as the ELSI journal club, peer writing group, and professional development seminars. I will also continue to attend professional development opportunities offered through the TraCS Institute and Office of Post-Doctoral Affairs. In order to better understand the probability calculations used in insurance, I will audit two classes through UNC's Department of Statistics and Operations Research: Introduction to Probability and Long-term Actuarial Models. I have taken these classes' prerequisites in my undergraduate and graduate training.

Training Justification: While I currently have strong skills in policy, legal, and basic quantitative analysis, I have no formal training in either quantitative or qualitative data collection methods. Learning qualitative case study methods and survey design will allow me to broaden my research scope and pursue promising research opportunities in the future. My legal and policy background naturally lead me to explore how societal concerns can be addressed through policies, regulations, or legislation. The ability to develop and conduct empirical research studies to better inform the subsequent legal and policy analyses will greatly benefit my future career and make me an independent researcher able to design research projects from a transdisciplinary perspective.

K99 Mentored Phase	Year 1											
Career Development Plan	S	O	N	D	J	F	M	A	M	J	J	A
Audit: Case Study Methods												
Audit: Odum Institute survey design courses												
AALS Qualitative Methods Workshop												
Audit: Introduction to Probability												
Odum Institute: Additional trainings												
CGS Trainee Group activities												
Individual/quarterly meetings with mentors												
Shadow mentors on GeneScreen												
Aim 1: International Case Studies	S	O	N	D	J	F	M	A	M	J	J	A
Case Study Screening Process/Selection												
Interview Guide Development												
IRB Submission for Interviews												
Recruitment to Case Study Participation												
Pilot Case Study (Canada)/Adjust Protocol												
Law & Society Ass'n (LSA) Conference												
Case Study Interview Conduction/ Analysis												
	Year 2											
Career Development Plan	S	O	N	D	J	F	M	A	M	J	J	A
Odum Institute: Additional survey trainings												
Audit: Long-term Actuarial Models												
TraCS Institute Mentoring Workshop												
CGS Trainee Group activities												
Individual/quarterly meetings with mentors												
Shadow mentors on GeneScreen												
Aim 1 Continued	S	O	N	D	J	F	M	A	M	J	J	A
Case Study Interview Conduction/Analysis												
ASBH Conference												
Preparation of Reports/Manuscripts												
Aim 2a: Survey of Ins. Commissioners	S	O	N	D	J	F	M	A	M	J	J	A
Survey Creation												
IRB Submission for Survey												
Survey Completion/Analysis												
LSA Conference												
Preparation of Manuscript												

Training in the Responsible Conduct of Research

Prior Training

During my graduate studies in law and public policy at Georgetown University, I was introduced to the history, theory, and regulatory framework of research ethics specific to the area of genetics and genomics research in two classes: “Contemporary Issues in Genetics and Society” and “Genetics and the Law”. Although I then spent three years practicing law in a legal services organization, once I entered a research setting I undertook formal training in the Responsible Conduct of Research (RCR). As a Postdoctoral Research Fellow at the Center for Genomics and Society at UNC I have engaged in several RCR trainings. On January 7, 2014, I took the Collaborative Institutional Training Initiative (CITI Program) on Human Research. This training covered the following topics: 1) History and ethics of human subjects research; 2) Basic Institutional Review Board (IRB) regulations and review process; 3) Informed consent; 4) Social and behavioral research (SBR) for biomedical researchers; 5) Records-based research; 6) Genetic research in human populations; 7) Research with protected populations; 8) Avoiding group harms; 9) FDA-regulated research; 10) Research and HIPAA privacy protections; 11) Vulnerable subjects; 12) Conflicts of interest in research involving human subjects; and 13) Privacy and confidentiality. Additionally, on February 26, 2014, I completed the UNC-CH Conflict of Interest training to learn about federal regulations that promote objectivity in research.

In addition to these online training, I also attended a five-day, four hours per day, in-person RCR training conducted by the TraCS Institute, the integrated home for the Clinical and Translational Science Awards (CTSA) program at UNC. This course provided training in the following topics: 1) Policies regarding human subjects research; 2) Principles for the ethical use of animals in research; 3) Safe laboratory practices; 4) Conflict of interest; 5) Mentor/mentee relationships; 6) Peer review; 7) Authorship and publication; 8) Data acquisition, management, sharing, ownership; 9) Research misconduct; 10) Collaborative research; and 11) Contemporary issues biomedical research. This training provided several opportunities for small group discussion of the topics using case studies.

Finally, throughout the past year I have attended many Research Ethics Grand Rounds (REGR), the monthly seminar series of local and invited speakers offered by the UNC Center for Bioethics in collaboration with the TraCS Institute and the Office of Research Ethics. These seminars address current ethical, legal, and social issues in the design and conduct of biomedical research involving human subjects. I have also attended a research ethics consultation through UNC’s Research Ethics Consultation Service.

RCR Training during K99/R00

During my award I will continue my training in RCR through four primary methods. First, I will attend a basic RCR training course, of at least eight hours in length, offered through either UNC’s Office of Postdoctoral Affairs or the TraCS Institute. Second, I will attend an RCR training provided by the TraCS Institute that is specifically designed for K awardees. This in person training includes four, two-hour meetings in which a faculty member or institutional official provides short lectures and guidance to develop a Responsible Conduct of Research (RCR) independent project. Participants are mentored in small groups of 5-6 participants with one facilitator per group. The participants are charged to identify an ethics or integrity issue in their own research, conduct a literature review, establish relevant rules and professional practice, consider alternative approaches through consultation with others, implement the plan or resolution, and practice teaching others in the seminar what was learned through a poster presentation. Among the topics identified and addressed to date have been plagiarism, clinical pre-screening, conflict of interest, informed consent, data sharing, documentation, authorship, and incidental findings, among others. Third, I will continue to attend the Research Ethics Grand Rounds at UNC. Fourth, during my regular meetings with my research mentors, Dr. Henderson, Dr. Skinner, and Professor Hall, we will identify and discuss any RCR issues related to my project. These experiences will continue to supply me with a robust training in the responsible conduct of research.

Description of Institutional Environment

During the training component of my K99/R00 grant, I will be based at UNC's Center for Genomics and Society (CGS), an NIH P50-funded "Center of Excellence in ELSI Research," housed within the Department of Social Medicine at the University of North Carolina at Chapel Hill. My primary mentor, Dr. Gail Henderson is Chair of the Department of Social Medicine and Director of CGS. Her office is located physically down the hall from my office, making informal check-ins and contact a weekly, if not daily, occurrence. Dr. Debra Skinner, my co-mentor, and Dr. James Evans, a member of my advisor committee, are also co-investigators with CGS.

Since its inception seven years ago, CGS has included a strong postdoctoral training program as one component of its mission to conduct transdisciplinary research on emerging ethical, legal, and social implications of genomic technologies. The goals of CGS's Training Program are to enable the trainees to: 1) acquire knowledge and skills needed to conduct ELSI research and translational work; 2) learn to work and communicate across disciplines; and 3) learn to communicate and disseminate ideas and findings effectively to academic, policy, and law audiences. CGS has fully funded eight post-doctoral fellows as formal CGS trainees. It has trained or is currently training eleven graduate students, six of whom received assistantships or developmental awards through CGS. It has also trained four undergraduates or recent graduates. In addition, CGS has involved sixteen other post-docs, graduate students, medical students, and law students in CGS research and training. All have gone to independent research and policy careers in their fields.

The CGS's postdoctoral scholars develop individualized training plans with their mentors, engage in research projects with the faculty co-investigators, conduct independent analyses and projects, and participate in a formal curriculum of professional development seminars, journal club discussions, and paper-writing groups. The current post-doctoral fellows, graduate students, medical students, and undergraduate students associated with CGS participate in these seminars creating an interdisciplinary and diverse group for discussion and feedback on writing. In addition, most trainees, including myself, have enrolled in courses on quantitative or qualitative methods through the Odum Institute for Social Science Research. Trainees have been funded to travel to national professional conferences and training workshops that provide networking and learning opportunities in their areas of interest.

The training environment at CGS is further enhanced by its affiliation with the Department of Social Medicine, an interdisciplinary department within the School of Medicine that also houses the UNC Center for Bioethics and the UNC Center for Health Equity Research. Each of these other Centers can offer training experiences, such as opportunities for fellows to become involved with the "Research Ethics Consultation Service" and the "Community Engagement Core" of the UNC TraCS Institute, the UNC Hospital Ethics Committee, and the "Bioethics at UNC" cross-campus faculty research group. Both the Center for Bioethics and the Center for Health Equity Research also host post-doctoral fellows, which gives the Department a combined cohort of 8-10 fellows at any one time, ranging across multiple disciplines.

This robust training environment in an interdisciplinary setting provides significant support for the transdisciplinary research and training demonstrated by this proposal. Additionally, this environment is well suited to enable productive collaboration between investigators, faculty members, and trainees. Since beginning my postdoctoral fellowship one year ago, I have co-authored papers with nine CGS investigators and trainees ranging in discipline from law to genetic counseling to sociology. During my K99 mentored phase of this grant, I will continue to benefit from the supportive interdisciplinary environment of CGS and the Department of Social Medicine.

Specific Aims:

In the US, there has been a polarized debate about whether life, long-term care, and disability insurers, referred to as 'supplemental' insurers, should be able to use an applicant's genetic information when setting rates or accepting policies. This debate usually references highly predictive and serious genetic diseases, such as Huntington's Disease or Lynch Syndrome. In reality, most variants have a wide range of predictive values, from unknown to low to high. There has been little debate about how predictive a variant must be for supplemental insurers to use—or to be legally allowed to use—the information. Additionally, for some highly predictive variants, medical interventions may be available to minimize one's indicated risk, and the law does not currently shed light on how insurers should consider this information. State unfair trade practice laws generally require insurers to have actuarial justification for using any risk factor in underwriting. Under these actuarial laws, to deny an application or charge an increased premium, insurers must show that a relevant risk factor is statistically associated with increased insurer cost. However, in the US, there has been little research regarding the application of these standards to genetic and genomic data. Internationally, several countries, such as the UK and Australia, have had actuarial policies for supplemental insurers specific to genetic testing since the early 2000s. Thus, most of the academic and policy discussions in this area have occurred abroad.

Although the Genetic Information Nondiscrimination Act (GINA) protects against genetic discrimination in employment and health insurance, individuals may fail to undertake medically recommended clinical genetic testing, or participate in genomic research, due to fears of discrimination in supplemental insurance. Policy responses tend to focus on whether supplemental insurers *should* be able to use genetic information, but do not explore the broader criteria that inform *when* and *how* such information can legally be used. Once studied, these criteria can inform a more nuanced policy discussion of the 'should'. This project has two primary goals: 1) to systematically examine the legal and policy landscape of supplemental insurer use of genetic information in the US and internationally, with particular focus on requirements of actuarial justification; and 2) to use these requirements to offer a variety of policy options for US state and federal governments that seek to address genetic discrimination in supplemental insurance. To meet these goals, I propose three specific aims.

Aim 1 – Analyze how international approaches to actuarial justification, supplemental insurance, and genetic information may be applicable to the US. Using methods and analysis techniques acquired during the mentored-phase, I will choose four countries that have robust policies regarding actuarial justification and insurer use of genetic information and conduct case studies of these examples. Focus on actuarial standards in the international privatized supplemental insurance sector ensures a more direct comparison with the US, despite differences across health insurance sectors. I will explore why specific policy options were chosen, whether these policies address issues related to predictive value or preventive measures, how effective the policies have been, and what lessons were learned. Case study analysis will combine both policy analysis and targeted interviews with key stakeholders such as academic/policy experts, government officials, advocacy group representatives, and insurance representatives.

Aim 2 – Interrogate how existing US state laws that require actuarial justification in supplemental insurance would apply to use of genetic information. Using multiple methods, I will explore how current state law may apply to genetic information. I will conduct a survey of US state insurance commissioners to examine how they are interpreting and enforcing actuarial and unfair trade practice laws (Aim 2a). I will combine this with legal analysis of statutes, regulations, and applicable case law to evaluate whether state law has been applied to the context of genetic information and how the laws may be interpreted and enforced in this area (Aim 2b). Survey responses will inform the legal analysis of how existing legislation may be enforced or interpreted.

Aim 3 – Provide policy analysis and recommendations for legislative and regulatory options to address concerns about the use of genetic information in supplemental insurance. I will undertake policy analysis of options available to US governments to address societal and individual concerns about supplemental insurer use of genetic information (Aim 3a). Additional policy analysis will explore legal and policy options for the threshold evidence levels needed to meet actuarial standards (Aim 3b). These options will incorporate feedback from policy experts. I will disseminate recommendations through policy briefs and manuscripts.

Aims 1 and 2a (**K99 phase)** will be completed in concert with training in qualitative and quantitative methods. For the **R00 phase**, my goal is to secure a tenured law position that involves teaching an experiential course and researching ELSI topics. Under this model, students will assist in the research goals of Aims 2b and 3.

By combining policy analysis and case studies from the international setting with detailed legal and survey analysis from the US, this project will produce a robust study of potential policy options for legislators.

Research Strategy

Significance

Imagine an individual who is known to have a genetic variant that was reported in a genome-wide association study (GWAS) to be weakly correlated with an increased risk of coronary artery disease, a leading cause of death worldwide. Should life, long-term care, or disability insurance companies be able to use this information in underwriting decisions, even if the genetic variant only explains about 1-2% of variation in risk? What if the variant explains 10% of risk? Or 80%? What if it explains 80% of risk, but there are measures that an individual can take to eliminate or mitigate this risk?

There has been a long-standing debate in the US regarding whether life, long-term care, or disability insurers, should be able to use genetic information in underwriting (Caulfield 2013, Joly 2013, Klitzman 2014, Ostrer 1993, Rothstein 1997). I refer to these insurers as supplemental insurers, in that they are purchased in addition to health insurance. I do not refer to health policies, such as a Medicare supplemental policy, that an individual acquires in addition to his or her existing health insurance. The supplemental insurer debates have often remained entrenched in discussion about whether or not insurers *should* be able to use genetic information (Mittra 2007). There has been little research and policy discussion of, if supplemental insurers have access to genetic information, *when* and *how* they should be able to use it in underwriting. This research project examines how law and policy address, or should address, the threshold of statistical significance between genetic information and increased risk necessary for insurers to charge higher premium rates or deny a policy.

In 2008, in response to the public's concerns of genetic discrimination, Congress passed the Genetic Information Nondiscrimination Act (GINA). GINA prevents employers and health insurers from using genetic information to discriminate, but does not regulate how supplemental insurers use genetic information (McGuire 2009). These insurers were not included in GINA due to political compromise and recognition that the economic models and social goals of supplemental insurance raise different policy considerations than health insurance (Hudson 2008). However, in the years since GINA's passage, individuals remain fearful of genetic discrimination in supplemental insurance (Allain 2012, Laedtke 2012, Parkman 2014). This fear may lead individuals not to undergo recommended clinical genetic testing or to decline participation in genomic research (Barlow-Stewart 2009, Feldman 2012, Joly 2010, Klitzman 2010, Peshkin 2013), potentially leading to detrimental health effects for those who do not undertake clinically beneficial testing (Otlowski 2012). Failure to undergo predictive testing for a medically actionable condition due to fear of discriminatory consequences could thwart an individual from preventing or mitigating disease.

Since federal law does not address supplemental insurer use of genetic information, any US-based policy in this area currently comes from state law. Several states address insurer use of genetic information (NCSL 2008). Three states are commonly cited as banning supplemental insurer use of genetic information (Peikoff 2014); in fact, these states do not completely prohibit insurer use, but rather, they prohibit use of family members' genetic information (O.R.S 2001, V.S.A. 1997) or have actuarial requirements for the use (Cal-GINA 2011, Chabner 2000). Requiring actuarial justification for use of genetic information in underwriting decisions, such as premium increases or denials, is a common legislative strategy. These laws generally require that insurers demonstrate statistical correlation between a risk and an increased likelihood of cost to the insurer (ASOP 2005, Jha 2012, Landes 2014). The interpretation, enforcement, and implementation of these actuarial laws, however, have not been fully analyzed. It is therefore surprisingly unclear how existing state laws have been or will be applied in the context of the predictive value and preventive measures of genetic variants.

Recent technological advances have drastically lowered the cost of sequencing, making genomic analysis potentially affordable for insurers. This information may be beneficial to insurers since underwriting involves categorizing applicants into risk classifications and genetic information can provide insight into future risk (Van Hoyweghen 2007). However, the use of genetic information also raises social concerns beyond the business considerations of insurers (Dubois 2011, Liukko 2010, Morris 2010, Moultrie 1997, Van Hoyweghen 2005, Van Hoyweghen 2012). For example, some, including myself, have argued or suggested that in order to fully address individual fears of genetic discrimination, supplemental insurers should be restricted from using genetic information (Ashcroft 2007, Gruber 2014, Klitzman 2014, Prince 2013, Wolf 2007). Others have argued that this would bankrupt the insurance system because it will skew risk classification and lead to adverse selection (Baker 2002, Dodge 2007, Green 2015, Joly 2010, Radetzki 2003, Rothstein 2004); yet there is little

empirical evidence of any effects of adverse selection following policy changes (Daykin 2003) and actuarial modeling has indicated low impacts on premiums (Macdonald 2011; 2010; 2003, Viswanathan 2007). The competing economic concerns of insurers and the privacy and justice concerns of individuals create polarizing interests and lead to an entrenched debate over insurers' use of genetic information (Joly 2010).

This proposed project is significant because it will provide policy-makers with in-depth analysis of policy and regulatory options and recommendations for how life, long-term care, and disability insurers use genetic information. The NHGRI has specifically identified use of genetic information by these supplemental insurance companies, determination of actuarial risk, and the impact of state laws as priorities for ELSI legal, regulatory, and public policy research (NHGRI 2014). Genomic technologies will not rise to their full clinical potential if fear of discrimination or misunderstanding of existing legal protections prevents individuals from undertaking genomic testing or participating in research. This project highlights lessons from international contexts; analyzes existing state legislation; and provides policy recommendations for future legislatures. Existing state laws offer an opportunity to suggest policy changes through a variety of mechanisms, from enforcement strategies to regulatory changes to new legislation. Providing meaningful and feasible policy options and a better understanding of how insurers can legally use genetic information can make several contributions: assuage fears of genetic discrimination, increase participation in genomic testing and research, and potentially prevent significant barriers in access to supplemental insurance. In turn, increased insurance coverage and utilization of genomic technologies can lead to greater economic stability and improved health for individuals.

Innovation

This proposal is original in its approach to the question of whether supplemental insurers should be able to use genetic information. By beginning the inquiry with how insurers can fairly or legally use such information, rather than if they should use it at all, this project can provide new insight to an entrenched US debate. Focusing on how international actuarial standards have been applied to genetic and genomic risk information allows this project to draw lessons from countries with distinct socio-historical contexts. Additionally, the proposed research project is innovative in the way that it combines legal and policy analysis with social science empirical analysis in a law school setting. Use of an experiential course model increases the amount of research that can be undertaken with the same amount of funding because students will provide research assistance as part of their experiential learning. Through this novel approach, I can simultaneously increase my chances of securing a position as an independent researcher, increase the impact of the project given the increased research that can be completed, and establish a mechanism to train future ELSI legal scholars. The proposal is also novel in its recognition of the importance of mentorship in the R00 phase and the inclusion of a specific professional development component on mentorship within the training plan.

Approach

Aim 1: Analyze how international approaches to actuarial justification, supplemental insurance, and genetic information may be applicable to the US.

Aim 1 Rationale: Several countries have long established policies that impose actuarial justification standards or regulate supplemental insurers in the context of genetic information. Because these countries often have universal health care systems that limit concerns of discrimination and access in the health care setting, policy discussions regarding concerns about genetic discrimination have focused on the supplemental insurances that are often privatized (Anderlik 2001, Knoppers 2004b). Compared to the US, these countries are generally more advanced in policy implementation in the context of supplemental insurance (Van Hoyweghen 2007).

There are three primary avenues that countries have used to address supplemental insurer use of genetic information (Knoppers 2004a, Lemmens 2003), although within these broad strategies there are a variety of types of policies (Joly 2010, Lemke 2013, Otlowski 2012, Quinn 2014, Varga 2012). First, insurers in some countries have voluntarily agreed to a moratorium on the use of genetic information for applications below a certain monetary value and to a requirement of actuarial justification for those above that value (Huijgen 2012, Soini 2012). For example, since 2001, supplemental insurers in the United Kingdom have had a voluntary moratorium, which was just recently extended to 2019 (HMG 2011, Thomas 2012). Second, some countries have passed legislation at the federal level requiring actuarial justification in this area (Soini 2012, Van Hoyweghen 2012). Utilizing this strategy, Australia has legislation that requires certain supplemental insurers to have actuarial justification for using genetic information (ALRC 2003, Keogh 2013, Taylor 2004). Third,

some countries have informal guidelines from a government advisory or regulatory body (Knoppers 2004a, Lemmens 2004). In these countries the guidance may not be legally binding on the insurers.

Exploration of the effectiveness of these approaches in the international context can provide lessons for policy implementation in the US. Although US states do have actuarial laws, there has not been robust policy discussion regarding how these laws may be enforced. As such, examining the international context first, where there have been debates, can inform the nuanced legal analysis of Aim 2. Although the health insurance systems across international contexts vary, the privatized supplemental insurance context provides a more directly comparable perspective to the US (Rothstein & Joly 2009). Specific focus on the standards of actuarial justification and the threshold levels of evidence needed to use genetic information in supplemental insurance underwriting also allows for an opportunity to gather lessons from international countries that have already been grappling with these nuances for many years, but without insurmountable concerns of applicability from differing socio-historical contexts. Through qualitative case studies of international experiences, Aim 1 will provide valuable information for the US-based policy analysis of Aims 2 and 3 of this project. Case study methods offer not only in-depth analysis of the individual cases but also analytic strategies for systematically comparing patterns observed across cases (Ragin 1999, Ragin 2014, Stake 2013, Yin 2003).

Aim 1 Methods: Aim 1 will utilize a qualitative, comparative case study analysis to explore how actuarial justification laws and policies in four countries have been applied to the use of genetic information in underwriting. Data sources include semi-structured interviews with stakeholders and analysis of policy documents, such as government reports or legislation, legislative history, internal government or insurance communications, legal case documents, and academic critiques or manuscripts regarding the policies. Each case study will utilize these multiple sources of data to allow for triangulation (Stake 2013, Yin 2003).

Initially I plan to conduct a pilot case study in Canada in order to test my interview protocol, determine the most efficient and effective ways to recruit stakeholders and collect data, and to confirm the feasibility of my case study methods. Canada is a fitting pilot study due to the proximity to the US, the robust discussions regarding actuarial justification policies that have occurred in the country to date (Joly 2006, Joly 2014, Lemmens 2010, Pullman 2010), and the support of a key stakeholder to assist with the identification and recruitment of other stakeholders (See Joly Support Letter). Canada has published guidance on use of genetic information in life insurance (Knoppers 2004b) and the legislature is currently considering a bill to ban insurer use of genetic information (Rennie 2013). Additionally, at the beginning of the project, I will undertake a screening process to select the remaining three purposively sampled cases (Yin 2003). These countries will be chosen to include representation of the three primary policy tactics (moratorium, legislation, or guidelines) utilized around the world. Cases will be selected that have had at least one policy mechanism in place for five years or more, have stakeholders with English language skills, and have similarities to the US for comparison.

I will explore the following research questions for each case study:

- Why was the particular policy option chosen in this country?
- How effective has the policy been, as judged by the stakeholders?
- How has the actuarial justification policy been applied to genetic information, specifically regarding the predictive value of genetic variants and the availability of preventive measures?
- Have there been any consequences, unexpected or expected, of the policy, and if so, what are they?
- From the stakeholders' perspectives, has the policy affected how often either individuals undertake genetic or genomic testing or apply for supplemental insurance?

Document Collection: Initially, I will collect policy documents and analysis available online through government websites and searches of academic databases such as LexisNexis, JSTOR, and PubMed. The CGS summer legal research assistant will assist with this task. However, since the availability of international documents may be limited in the US, I will also establish meetings with government and research librarians in the case study countries to gather additional relevant documents unavailable in the US. During each interview, I will also ask the respondents for suggestions of documents the respondent thinks might be informative to the study.

Interviews: Employing the skills I will acquire through focused trainings on qualitative interview design, I will create and conduct semi-structured interviews with key stakeholders (King 2010). For each case study I will interview at least 8 stakeholders representing policy experts, government officials, advocacy group members, and insurance representatives. To the extent possible in each country I will speak to at least two stakeholders

from each category. This targeted interviewing of a diverse group of stakeholders is important for minimizing single-source information bias, maximizing the range of perspectives, and collecting differential knowledge (Van de Ven 1999). These stakeholders will be identified through help from my international contacts (See De Paor, Joly, and Macdonald Letters), policy documents and research, and suggestions from individuals who have agreed to be interviewed. Although this approach has the potential to create a participant population skewed to one perspective, this will not be likely since the nature of policy discussions inevitably highlight diverse opinions. Therefore, already identified policy-makers and key stakeholders are likely to know, and will be asked to identify, individuals with a broad range of perspectives and opinions. They will be enrolled through a recruitment letter and follow-up phone call. I will pilot test my data collection protocol and semi-structured interview guide in Canada, and then conduct the three additional case studies. Interviews will be conducted in person to ensure convenience for the participants, quality of the interview, minimization of technological complications, and ease of document collection pre and post-interview (See Foreign Justification).

Data Analysis: I will undertake content analysis of the interview transcripts utilizing software, such as ATLAS.ti, that aids in this kind of analysis. I will be trained in content analysis through classes at the Odum Institute, AALS Qualitative Workshop, and ResearchTalk. I will also pursue my analysis by comparing the content of the policy documents collected with the themes extracted from the interviews.

Aim 1 Expected and Alternative Outcomes: For each country studied I will develop a written overview that includes: 1) a descriptive summary of the policy method(s) implemented and the context in which it was implemented, 2) a description of how actuarial justification standards have been applied to genetic information, 3) an overview of how effective the policy has been according to documents and interview respondents, and 4) an assessment of the benefits and challenges of each policy. After individual case analysis, I will perform a cross-case analysis, examining whether the application of actuarial justification standards differs across policy options. To disseminate these research findings I will publish at least one manuscript summarizing the case study research findings. Additionally, I will present my findings at national conferences such as the American Society for Bioethics and Humanities (ASBH) and the Law and Society Association (LSA).

International policy analysis and recruitment for interviews can be challenging; however, I believe that I will be able to recruit adequate numbers of interview participants. There is robust scholarship regarding actuarial justification policies and genetic information in the international setting, making it likely that I can find willing and interested participants to discuss the implications of these policies. Additionally, through my previous work and through support of my advisory committee members, Drs. De Paor and Macdonald, I have connections to the European genetics communities, and through my collaborator Dr. Joly, the Canadian community (See Support Letters). Thus, I will be able to reach out to a variety of contacts for suggestions of key stakeholders.

By undertaking a pilot feasibility case study and by waiting to choose the remaining three case study countries until the project is underway, I can foresee and avoid problems related to recruitment of stakeholders or conducting the case studies. If I am unable to gather sufficient research participant interest in a country, I will choose a different option for the case study. Additionally, if the Canadian pilot study highlights problems with the initial case study design I can rework the protocol with support from mentors for the remaining cases.

Aim 2 – Interrogate how existing US state laws that require actuarial justification in supplemental insurance would apply to use of genetic information

Aim 2 Rationale: Under state unfair trade practice laws, life insurers in all fifty states are required to have actuarial justification to use a risk factor in underwriting (Holmes 1996, McEwen 1993, UTPA 2004). Some states have expanded these rules to disability and long-term care insurers (Avraham 2014). In addition, eight states explicitly require actuarial justification for the use of genetic information in underwriting (NCSL 2008). These laws aim to restrict supplemental insurers from basing underwriting decisions on genetic information that is unrelated to risk. However, the genetic-specific actuarial justification laws likely do not provide any additional protections for individuals beyond the broader unfair trade practice laws (Rothstein 2007).

These state laws, both the genetic-specific and general unfair trade practice laws, have not been fully explored and further research is needed to understand how these rules will be applied in the context of genetic variants. Given the range of predictive value of genetic variants, it is uncertain how many will be sufficiently correlated to risk to meet actuarial standards (Evans 2001, Janssens 2006, Macdonald 2002) and how the preventive measures available to mitigate risk will and should fit into the legal actuarial standards (Keogh 2013). Although

insight into these questions will come from the international data obtained in Aim 1, it is also important to understand how the US state laws are being applied, and most significantly, could be applied, in this context.

Insurance companies, including life, long-term care, and disability insurers, are regulated through state insurance commissioners and in every state the insurance commissioner has the power to enforce state insurance laws and promulgate regulation (Randall 2008). The commissioner offices also provide services to consumers of these insurances through information and complaint systems (NAIC 2011). Through their work with both insurers and consumers, the insurance commissioners are an essential source of information for how actuarial justification laws are being used. Through surveys of state insurance commissioners, and legal analysis of state law, regulation, and court cases, Aim 2 will provide an opportunity to better understand how actuarial justification and unfair trade practice laws are currently being enforced and implemented in the US.

Aim 2 Methods: Aim 2 will employ multiple methods to analyze US actuarial justification laws and will involve two sub-aims: Aim 2a will survey state insurance commissioners to determine how they are enforcing and interpreting actuarial justification laws; based on survey results, Aim 2b will undertake a legal analysis of current state actuarial justification and unfair trade practice laws. There are already a handful of cursory state law reviews that will inform the survey (CLRC 2012, CRG 2014, NCSL 2008). I am proposing to undertake the in-depth legal analysis after the surveys in order to conduct a more nuanced and detailed legal analysis.

Survey: For Aim 2a, I will develop and implement a survey of state insurance commissioners about actuarial and unfair trade practice laws and how the commissioners interpret and enforce these laws. The survey will focus on genetic information, the low predictive value of most variants, and the preventive measures available for some genetic variants. Surveys and interviews of insurance commissioners have been used in prior studies to understand how health and life insurers could use genetic information, including a case study analysis completed by my co-mentor Prof. Hall (Hall 2000a, Hall 2000b, Hall 2000c, McEwen 1992). Aim 2a survey questions will be developed in concert with feedback from mentors and based on survey methodology trainings undertaken through the Odum Institute. In addition to questions on how current state laws are interpreted and enforced, the survey will include questions that draw upon policy themes discovered during Aim 1. It will include both closed and open-ended questions surrounding these themes. The surveys will be sent to all state commissioners and follow-up letters and phone calls will be made to reach state offices that have not responded. In a prior study surveying state commissioners, this method was found to lead to a remarkably high response rate (82.4%) (McEwen 1992). The CGS legal research assistant will assist with survey analysis and follow-up on any laws cited by the commissioners. To disseminate the survey results, I will publish findings in peer-reviewed journals, and use the information about enforcement and interpretation to assist with the legal analysis of Aim 2b. Additionally, I will present my work at national conferences such as ASBH and LSA.

Legal Analysis: For Aim 2b, I will conduct a fifty state review of laws, regulations, and court case decisions (case law) relating to actuarial justification, both genetic-specific and broader unfair trade practice laws. I will specifically explore whether and how actuarial standards are defined and whether genetic-specific actuarial justification laws provide, or potentially provide, protections beyond those the state unfair trade practice laws. If the plain text of the statute or regulation is unclear, I will employ statutory interpretation methodology I learned when I took the “Lawmaking and Statutory Interpretation Seminar” taught by Congresswoman Eleanor Holmes-Norton. This state review will provide a comprehensive guide to which state laws apply to which supplemental insurers. Several organizations have completed state guides regarding state laws covering genetic information in supplemental insurance (CLRC 2012, CRG 2014, NCSL 2008) and other sources have information on state unfair trade practice laws (Avraham 2014, Holmes 1996); however no study has combined information about how all these laws may work in practice, with specific focus on whether and how actuarial standards are defined. These previous guides will form my starting data points, so my initial data collection will involve updating available cites, rather than a new search. In addition to this background analysis of state laws and regulations, Aim 2b will use legal analysis to examine applicable case law to evaluate whether state law has been used in the context of genetic information and how the laws may be interpreted and enforced in this area. Both the state statutes and the case law will be compiled through searches of WestlawNext, a legal database.

The specific questions of inquiry in the case law analysis will include:

- Is there any case law explicitly addressing genetic information and actuarial justification or unfair trade practice laws?

- Does past case law define or discuss actuarial standards or address what level of statistical correlation is necessary for insurers to use risk factor information in underwriting?
- How might precedential case law regarding medical information or disability be applied in the context of genetic information?
- Is there any case law that discusses how supplemental insurers should take into account mitigating risk factors, such as available preventive measures?

Aim 2 Expected and Alternative Outcomes: Aim 2a will culminate in at least one published manuscript summarizing the state insurance commissioner survey design, methodology, and results. To disseminate the information from Aim 2b I will complete a published law review article describing the findings of the statute, regulation, and case law analysis. I am expecting to find that the genetic-specific actuarial justification laws do not provide any additional legal protections beyond state unfair trade practice laws. Additionally, I am expecting that few cases will explicitly address genetic information in this arena. However, because the genetic-specific and unfair trade practice laws are likely similar, case law regarding how unfair trade practice laws have applied to other medical information provides important legal precedent for how future courts will apply these laws to the context of genetic information.

Analysis of statutes in fifty states can be time consuming to complete and, depending upon the volume of applicable or precedential case law, the case analysis can also be time consuming. However, these tasks of Aim 2b will be completed during the R00 phase of the project. During this phase, my goal is to have students assist with the data collection and analysis as part of their experiential class. This model will allow for sufficient research support to complete the full fifty state analysis. If, however, I am unable to secure this teaching opportunity and/or do not have sufficient research support to analyze the case law and statutes from all states, I plan to limit the number of states that I examine to a representative sample.

Aim 3 - Provide policy analysis and recommendations for legislative and regulatory options to address concerns about the use of genetic information in supplemental insurance.

Aim 3 Rationale: Since the passage of GINA, there has been discussion of whether the federal government should pass additional legislation that expands protection against genetic discrimination in supplemental insurances. There are strong competing interests on both sides of this debate: Individuals fear the misuse of their genetic information and supplemental insurers fear the economic consequences and adverse selection in their businesses (Daykin 2003, Haidle 2014, Macdonald 2002, Rothstein & Joly 2009). These competing views create difficult policy decisions for state and federal legislators. However, international and US state experiences to date can provide valuable insight into the feasibility, implications, and benefits of various policy options. Aim 3 of this project will synthesize information and data collected through Aims 1 and 2 to create policy analyses and reports of various options, including the moratorium, legislative, and guideline options from the international context. Aims 1 and 2 will help to better understand the varying interpretations of the levels of evidence needed to meet actuarial justification and unfair trade practice laws. From there, Aim 3 can provide policy guidance to state insurance commissioners, state legislators, individuals, insurance companies, and advocates about enforcement, interpretations, and legal uses of genetic information in underwriting.

Aim 3 Methods: Using policy analysis skills I developed during my graduate training in my Masters of Public Policy, Aim 3 will include two levels of policy analysis and inquiry. First, Aim 3a will be a policy analysis of the legislative options available at the federal and state level to address supplemental insurer use of genetic information, ranging from status quo to a complete ban on use, and other options in between. The analysis will include an assessment of the potential limitations, benefits, and feasibility of various policy options.

The policy analysis will explore the following questions:

- Do current state policies effectively address supplemental insurer use of genetic information?
- Is additional, or different, enforcement of current state laws needed to afford effective protection?
- Would any of the policy mechanisms implemented in the international context be options for US federal or state governments?
- What are the limitations, benefits, and feasibility of various policy options?

Second, Aim 3b will assess how both international case studies and the states define evidence thresholds for the necessary level of statistical correlation to use genetic information in underwriting. I will conduct policy

analysis of these varying interpretations and actuarial definitions to assess the implications of various evidence thresholds. If there have not been clear evidence thresholds or if the thresholds are consistent, I will assess the implications of what the threshold could or should be. This will provide policy makers, insurance companies, insurance commissioners, and individuals undergoing genetic testing guidance on when and how genetic information can and should legally be used for underwriting. In order to receive feedback and suggestions on various policy options, I will vet options with US policy experts, such as Dr. Koontz, my advisory committee member, to discuss issues of actuarial justification, genetic information, and supplemental insurance.

As with Aim 2b, the research of Aim 3 will be completed within the R00 portion of the grant; therefore my goal is to complete this research within the context of the experiential class at a law school. The assistance of students in the legal and policy analysis creates the ability to increase the output of policy analysis to potential state-specific white papers or other in-depth policy analysis given findings from the previous Aim(s).

Aim 3 Expected and Alternative Outcomes: Aim 3 will culminate in a series of policy briefs, or white papers, that legislators at the federal and state levels can utilize. These briefs will be disseminated to the state insurance commissioners who participated in Aim 2 in order to have maximum impact. Discussions and feedback from policy experts will also be incorporated into the policy reports as well as compiled into a manuscript summarizing the key recommendations of the group. I will write at least one law review or peer-reviewed journal article summarizing the policy findings of the project in order to disseminate the information to a wider audience. I will also attend conferences, such as ASBH and LSA, to present my work.

Although Aim 3 will draw largely on the information gathered during Aims 1 and 2, the research and analysis of Aim 3 is not dependent upon a certain outcome in the previous aims. Even in the unlikely event that there is little information gathered on the interpretation of actuarial and unfair trade practice laws, this absence of guidance still provides a critical opportunity to explore possible options for the future.

Since the policy analysis of Aim 3 will occur in Years 4 and 5, it is possible that new state or federal legislation may be passed before the final years of the grant. I will track any changes in policy throughout the grant period. If changes occur, the skills gained during the K99 training will allow me to alter the policy analysis as needed. For example, if federal legislation addressing supplemental insurer use of genetic information is passed during the grant, I can conduct a case study of the new legislation to assess enforcement options, issues that can be addressed by ensuing regulation, and the potential effectiveness of the law.

Through detailed policy and case study analysis from the international setting and robust legal and survey analysis from the US, my proposed K99/R00 will recommend potential policy options for supplemental insurer use of genetic information, thus supporting and informing an important NHGRI ELSI research priority.

R00 Independent Phase Research	Year 3											
Aim 2b: Legal Analysis of State Statutes and Cases	S	O	N	D	J	F	M	A	M	J	J	A
Collect Statutes/Regulations through WestLaw												
Statute and Regulation Analysis												
Collect Case Law through Westlaw												
Case Law Comparison and Analysis												
Cross Comparison of Case Law/Statutes/Survey Results												
Dissemination at Conferences												
	Year 4											
Aim 2b: Legal Analysis of State Statutes and Cases	S	O	N	D	J	F	M	A	M	J	J	A
Preparation of Law Review												
Aim 3a and 3b: Policy Options	S	O	N	D	J	F	M	A	M	J	J	A
Identification of Policy Options from Aims 1 and 2												
Policy Analysis 3a												
Identification of Actuarial Standards from Aims 1 and 2												
Policy Analysis 3b												
Dissemination at Conferences												
	Year 5											
Aim 3b: Actuarial Justification Standards Policy Options	S	O	N	D	J	F	M	A	M	J	J	A
Preparation of Policy Brief(s)												
Preparation of Manuscript												
Dissemination at Conferences												
Grant Applications for Continued Independent Research												

Protection of Human Subjects

Risks to Human Subjects

Human Subjects Involvement, Characteristics, and Design

This project explores policy options for addressing life, long-term care, and disability insurer use of genetic information in underwriting. In furtherance of this overall goal, Aims 1 and 2a seek to gather information about how international countries and US state governments are approaching, interpreting, and enforcing actuarial justification standards in their respective contexts. Human subject involvement is a necessary component of these aims in order to gain a nuanced perspective of the standards from a variety of groups involved in policy and its effects.

For Aim 1, I plan to recruit approximately eight academic/policy experts, government officials, advocacy group representatives, and insurance representatives from Canada for the initial pilot case study interviews and recruit approximately 24-30 individuals (8-10 per country) in these categories for interviews from three additional case study countries. The exact location of these case studies will be determined given initial research into possible case study options; however, it will likely be two European Union countries and one non-European Union country due to the large number of countries in Europe that have policies in this area. Cases will be selected that have had at least one policy mechanism in place for at least five years; have stakeholders with English language fluency, and have similarities to the US for comparison.

As part of the case studies, I will perform in-person, semi-structured interviews with participants. Given the professional nature of the work positions from which I am recruiting, these individuals will be adult women and men. Respondents' characteristics will reflect the gender and race/ethnicity of the individuals who are employed by governments or insurance companies, or who are ELSI scholars, advocates, or policy makers in each country. These individuals will not be paid for participation in the interviews.

For Aim 2a, I plan to recruit 51 US state insurance commissioners, or the appropriate staff member in the insurance commissioner office, for a survey on state actuarial justification laws. Similar to Aim 1, given the professional nature of the work positions from which I am recruiting, these individuals will be adult women and men. Respondents' characteristics will reflect the gender and race/ethnicity of individuals who are state insurance commissioners or who are employed by state insurance commissioner offices.

For both Aims, no vulnerable populations are included in this recruitment plan. Recruitment will take place at the University of North Carolina at Chapel Hill (UNC) via email, letter, and phone to US state and international participants. Additional recruitment for the stakeholder interviews may also occur on location. Stakeholder interviews will occur in person. The state insurance commissioner surveys will be completed remotely via an online system such as Qualtrix and results will be electronically returned to UNC.

Sources of Materials

Data collected from human subjects include survey responses; digital audio recordings and transcriptions of in-person interviews; and policy documents and materials provided by the case study participants and others.

Aim 1 Interviews: Confidentiality will be maintained in several ways. First, digital voice files will be stored on a protected server and deleted once transcribed. Transcripts will be de-identified by a unique code number for each participant and the de-identified files will be stored on a protected server and accessible only to the me and other individuals assisting with the research as needed. The list linking this code to the participant's name and contact information will be kept in a password-protected file on a secure server. Participant's real names will not be used in any publication related to the study.

Aim 2a Surveys: Survey results will be stored electronically on a secure server. Any paper copies returned via mail will be stored in a locked file cabinet. Given the nature of the survey results and analysis, state-specific responses may be included in analysis or publications. Although the specific names of the individual who completed the form will not be included in any publications, because there is only one survey respondent per state, it may be possible for a reader to identify the respondent given that the identity of insurance commissioners and their staff members are publicly available information. However,

the survey will include questions only about the respondents' professional capacity and opinions, therefore harms are minimized (see below).

Potential Risks

The risks to respondents for both Aim 1 interviews and Aim 2a surveys are minimal. The questions are primarily factual in nature, asking about how and why a policy mechanism was chosen, how nuances of the policy have been implemented and enforced, and how effective the policy has been. The respondents will be chosen based upon their professions and involvement in policy-making. As such, they will be accustomed to addressing questions of policy development and effectiveness, including those that could be construed as potentially controversial. The subject matter of the interviews and surveys is limited to policy issues regarding insurer use of genetic information: No personal demographic information will be collected beyond job title, description, and work contact information. Respondent responses are limited to their views, disciplinary or professional based perspectives, opinions, and experience with regard to the policy subject matter. Thus, even inadvertent breaches of confidentiality will pose no risk with regard to participants' financial standing, employability, legal liability, or reputation.

Adequacy of Protection Against Risks

Recruitment and Informed Consent

Aim 1 Interviews: Recruitment for the four case studies will begin with an identification of the key stakeholders involved in policies regarding insurer use of genetic information. In this process members of my advisory panel and other collaborators will assist me to identify the sufficient breadth of stakeholders (See Joly, De Paor, and Macdonald letters). Additional participants will be collected by asking interviewees: Each person who responds to an interview request will be asked to identify any additional individuals who are key stakeholders in these policy discussions. I will obtain informed consent prior to the start of the interviews. This consent will include the purpose of the study, the nature of the subject's participation, the possible risks and discomforts associated with participation, the potential benefits of participation, a statement of the voluntary nature of participation, and a description of the mechanisms used to ensure confidentiality.

Aim 2a Survey: The survey invitation will initially be sent to the state insurance commissioner of each state and the District of Columbia. Follow-up letters and phone calls will be conducted to reach those state offices that have not responded. If the state insurance commissioner is unavailable or unable to complete the survey, I will contact a targeted staff member in the insurance commissioner's office, such as the highest ranked employee in charge of policy or consumer complaints. The survey will completed over the web using survey programs, such as Qualtrix. Informed consent will be obtained at the start of the web survey.

For both aims, participation in any interviews and surveys is voluntary. Depending on the final interview guide and survey questions, I may request Exemption 2 (45 CFR 46.101(b)(2)) in the IRB application for these aims.

Protections Against Risk

Procedures for protecting against or minimizing potential risks, including risks to privacy of individuals or confidentiality of data are as follows: Contact information for the interview and survey participants will be maintained in separate files. Before any interview commences, participants will be asked to choose a location within their office for the interview that ensures sufficient privacy. Survey and interview data will be assigned codes, and links to contact information and/or individually identifiable private information about human subjects will be removed from all other documents except the code key. Only I will have access to the code key. While I do not anticipate that the interview or survey questions will be perceived as sensitive, respondents will be told of the procedures to protect privacy and confidentiality, and in the event that they express concerns, I will remind them that they should feel free to skip any questions or withdraw from the interview at any time. Participants' names will not appear in any study publications.

Potential Benefits of the Proposed Research to Human Subjects and Others

There are no individual benefits to participants in this study. However, potential burdens are small, mainly the time involved in participating in the survey or interviews. My plan to disseminate study findings and to use them for policy recommendations may be perceived by some as a long-term benefit. These possible benefits are small but proportional to the minimal risks associated with study participation.

Importance of the Knowledge to be Gained

The information to be gained through this project has the potential to fill important gaps in policy guidance for life, long-term care, and disability insurer use of genetic information. The NHGRI has identified questions regarding supplemental insurer use of genetic information, including questions regarding actuarial justification, as an ELSI research priority. Additionally, there has been increasing discussion regarding whether federal legislation is needed to address use of genetic information by these insurers; however, the current US debates on the topic have been relatively narrow. This project will provide more nuanced perspectives to guide future policy discussion. Increased understanding of how insurers can, and should legally be allowed to, use genetic information may decrease fear of discrimination and thus lead to increased participation in genomic research and clinical testing across society. Minimal risks to subjects are reasonable in relation to the importance of the knowledge that reasonably may be expected to result.

Data and Safety Monitoring Plan

N/A

Inclusion of Women and Minorities

Individuals in this study will be recruited based upon the professional role they hold, not upon demographics. Given the case study nature of the proposed study, there will be no opportunity to enrich the interview samples beyond the existing demographics of the planned cohorts. Therefore, the gender and racial composition for this study will be determined by the professional population of policy experts, government representatives, insurance representatives, advocacy group representatives, and academics for the case studies and the current insurance commissioners and employees for the survey. This project will make every effort to include women and minorities in every component of the study when possible.

OMB Number: 0925-0002

Planned Enrollment Report

Study Title: Use of Genetic Information by Life, Long-term Care, and Disability Insurers: Exploring International Lessons, the Domestic Legal Landscape, and Options for U.S. Policy: Aim 1

Domestic/Foreign: Foreign

Comments: This project will recruit approximately 48 stakeholders from 4 different countries for in-depth interviews as part of a case study analysis. The stakeholders will be made up of policy experts, government officials, advocacy group members, and insurance representatives, with at least two representatives from each category in every country. This project will strive to enroll a diverse sample of participants; however the individuals will be recruited based on their professional role, not base

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/Alaska Native	0	0	0	0	**0**
Asian	3	3	0	0	**6**
Native Hawaiian or Other Pacific Islander	1	1	0	0	**2**
Black or African American	3	3	0	0	**6**
White	10	10	2	2	**24**
More than One Race	3	3	2	2	**10**
Total	**20**	**20**	**4**	**4**	**48**

Study 1 of 2

Funding Opportunity Number: PA-15-083. Received Date: 2015-02-11T15:56:35.000-05:00

OMB Number: 0925-0002

Planned Enrollment Report

Study Title: Use of Genetic Information by Life, Long-term Care, and Disability Insurers: Exploring International Lessons, the Domestic Legal Landscape, and Options for U.S. Policy: Aim 2

Domestic/Foreign: Domestic

Comments: This project will survey the state insurance commissioners from the 50 states and the District of Columbia. Thus, the gender and racial composition for this study with be determined by individuals who hold the office of insurance commissioners.

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/Alaska Native	0	0	0	0	**0**
Asian	0	0	0	0	**0**
Native Hawaiian or Other Pacific Islander	0	1	0	0	**1**
Black or African American	0	1	0	0	**1**
White	12	36	1	0	**49**
More than One Race	0	0	0	0	**0**
Total	**12**	**38**	**1**	**0**	**51**

Study 2 of 2

Funding Opportunity Number: PA-15-083. Received Date: 2015-02-11T15:56:35.000-05:00

Exclusion of Children

The research topic to be studied is not relevant to children.

Supplemental Materials for NIH Application # 1K99 HG008819-01
Use of Genetic Information by Life, Long-term Care, and Disability Insurers: Exploring International Lessons, the Domestic Legal Landscape, and Options for U.S. Policy
PD/PI: Prince, Anya

Publication updates – Recently accepted articles

Unpublished

Unpublished