

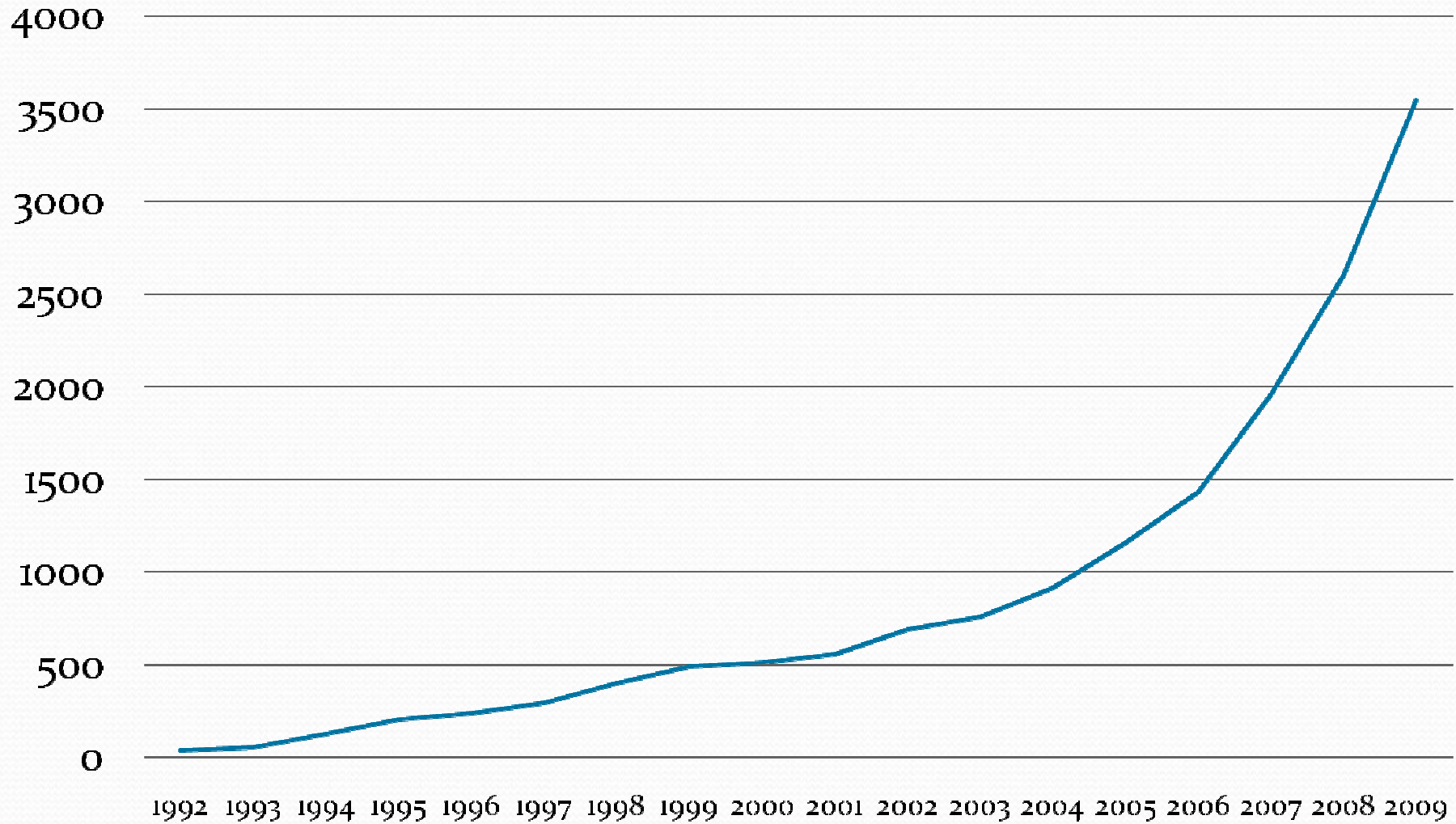
Biomarker Studies in Low and Middle Income Countries

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Biomarkers?

- Originally used to denote a biological substance used in some way to examine health
- Expanded to include anything that measures health
 - Including anthropometrics, blood pressure, grip strength, etc.
- What's being marked or measured?
 - Risk factor, outcome, process, variation

“Biomarkers” Articles



Web of Science

Answering Questions

- Not very interesting on their own
- Combined with other data can be used to understand mechanism of aging
 - As a marker or measure
 - Risk factor, process, outcome or link
- Need to understand which biomeasures should/can be used to answer specific questions

What can be analyzed?

- Clinically relevant and experimental measures/markers
- Sources of physiological measures/markers
 - Blood
capillary or venous
 - Saliva
 - Urine
 - others

Capillary Blood Collection

- Minimally invasive
- Minimal processing
- Better portability



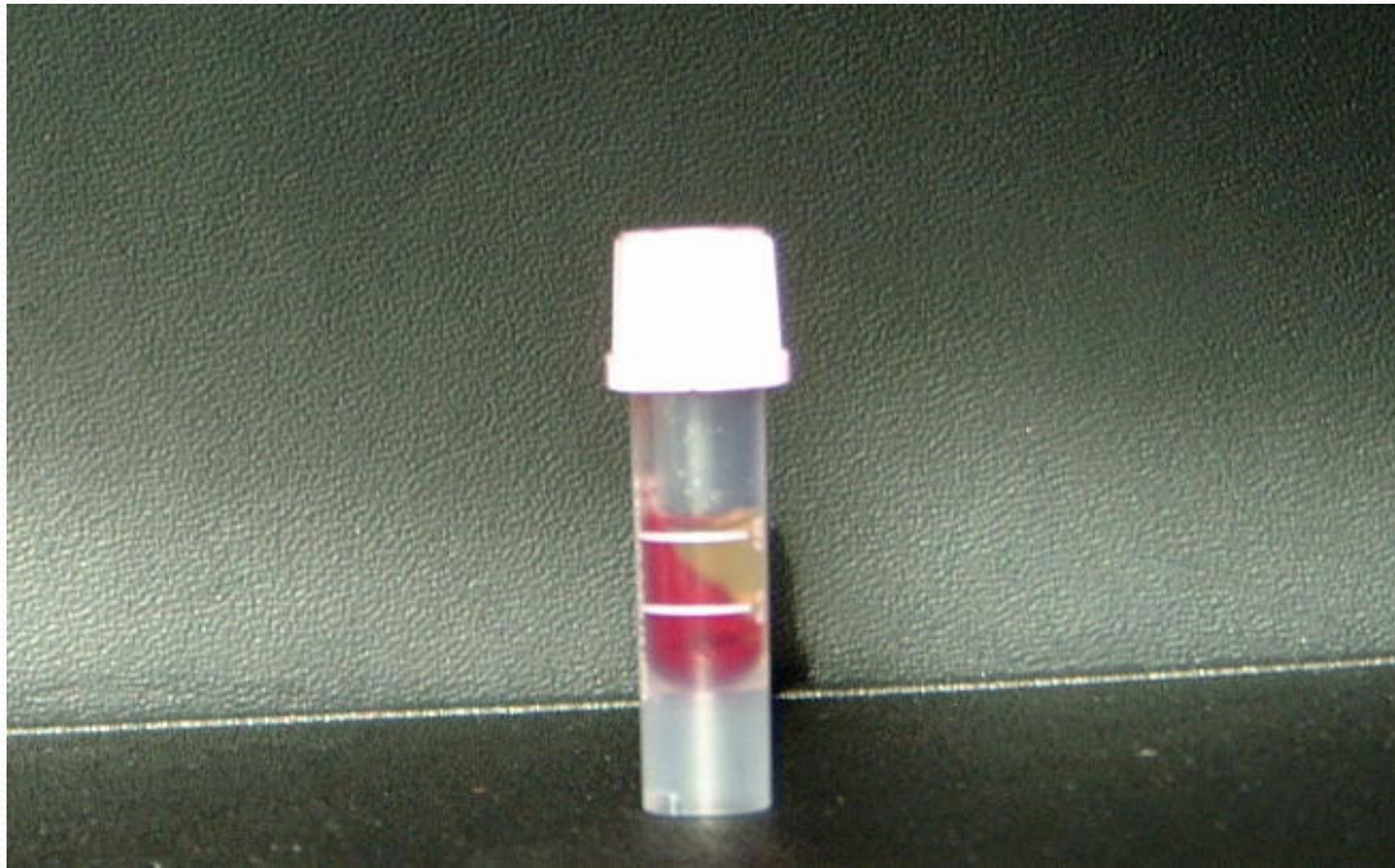
Method: Point of Care



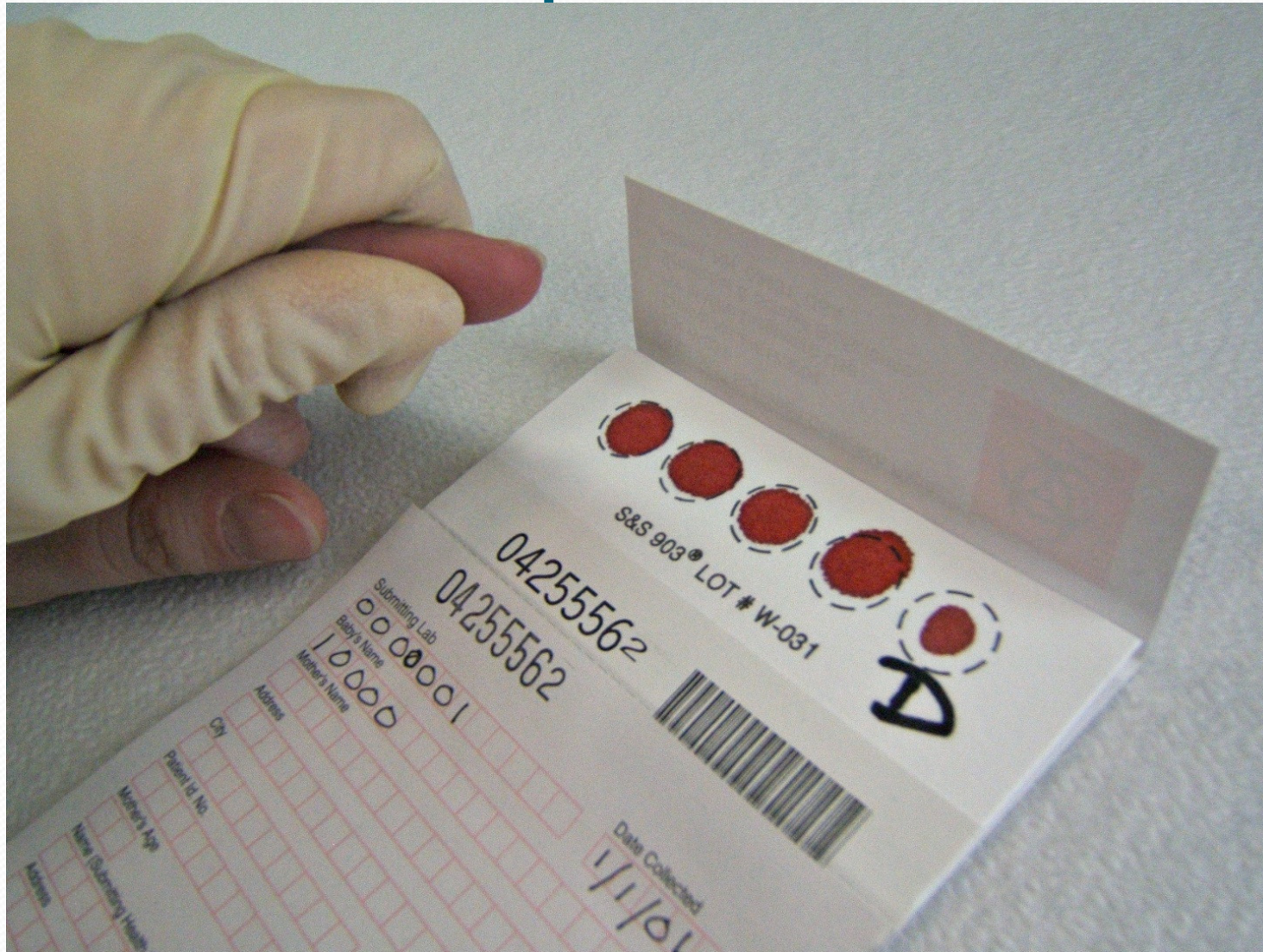
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Capillary Tube Collection



Dried Blood Spots



What can be done?

- In theory...
 - Anything that can be analyzed from venous blood
 - Short half-life
 - Interference
 - “sticky” proteins
 - Continuing physiological reaction (i.e. continued glycosylation)
 - Similar methods
 - Enzyme-linked immunosorbent assay (ELISA)
 - Radioactive immunoassay (RIA)
 - Bead-based technology (i.e. luminex)

Appendix 1. List of analytes that have been analyzed in dried blood spot (DBS) samples (not including analytes listed in appendix 2).

Analyte	Reference
Acylcarnitines/ Carnitine	(Chace, Hillman et al. 1997; Heinig and Henion 1999; Schulze, Schmidt et al. 2003)
Amino acids	(Zytkovicz, Fitzgerald et al. 2001; Deng, Deng et al. 2002; Deng and Deng 2003)
Alpha-fetoprotein	(Mizejewski, Bellisario et al. 1982; Parkinson, McMahon et al. 1996)
Amodiaquine/ Desethylamodiaquine	(Gitau, Muchohi et al. 2004)
Biotinidase	(Yamaguchi, Fukushi et al. 1987; Pettit, Amador et al. 1989; Broda, Baumgartner et al. 2001)
Brucella antibodies	(Takkouche, Iglesias et al. 1995)
Ceruplasmin (Wilson's disease)	(Ohura, Abukawa et al. 1999)
Chloroquine/ Chlorpheniramine	(Okonkwo, Coker et al. 1999; Minzi, Rais et al. 2003)
Cocaine (Benzoyllecgonine)	(Henderson, Powell et al. 1997)
Cysticercus antibodies	(Peralta, Macedo et al. 2001)
Cytokines (multiple)	(Phillips and Krum 1998; Nelson, Grether et al. 2003)
Dichlorodiphenyldichloroethylene	(Burse, DeGuzman et al. 1997)
Dihydropteridine reductase	(Jeeps, Silcox et al. 1986)
Diphtheria/ Tetanus antitoxin	(Arya 1989; Hong, Ke et al. 1996)
Erythrocyte protoporphyrin	(Orfanos, Murphey et al. 1977)
Fatty acids/ Acylglycines	(Schmidt-Sommerfeld, Penn et al. 1993; Bennett, Ragni et al. 1994; Bonham Carter, Watson et al. 1996; Johnson 2000; Kimura, Yoon et al. 2002)
Filariasis antibodies	(Terhell, Haarbrink et al. 1996)
Galactose/ Galactose-1-phosphate	(Orfanos, Jinks et al. 1986; Hong, Yoon et al. 2001)
GALT	(Rhode, Elei et al. 1998; Fujimoto, Okano et al. 2000)

McDade TW, Williams SR, Snodgrass JJ. 2007. What a drop can do: Dried blood spots as a minimally-invasive method for integrating biomarkers into population-based research. *Demography* 44: 899-925.

HOWEVER...

- Just because it has been done, doesn't mean it is feasible or even possible
 - Depends on availability of:
 - Protocols
 - Materials
 - Equipment
 - Reproducibility and validity
 - Cost is always an issue

What has been done?

Table 1. Recent applications of dried blood spot (DBS) sampling in large population-based studies in the U.S..

Study	N ^a	Age range	Biomarkers in DBS
Great Smoky Mountains Study	1,071	9-15 years	Androstenedione, DHEA-S, EBV antibodies, estradiol, FSH, LH, testosterone
Health and Retirement Study	7,000 ^b	>50 years	CRP, HbA1c, Total cholesterol, HDL
Los Angeles Family and Neighborhood Survey	5,000 ^b	3 years and up	CRP, EBV antibodies, HbA1c, Total cholesterol, HDL
National Longitudinal Study of Adolescent Health	17,000 ^b	32-31 years	CRP, EBV antibodies, HbA1c
National Social Life, Health, and Aging Project	1,945	57-84 years	CRP, EBV antibodies, HbA1c, hemoglobin

^aFor DBS sampling

^bProjected

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The National Social Life Health and Aging Project (NSHAP)

- Understand the relationship between social support, personal relationships and health in older adults
- Interview 3,005 community-residing adults
- Population-based sample with minority over-sampling
- 120-minute in-home interview
 - Questionnaire
 - Biomeasure collection
 - 2,044 individuals (84.5% cooperation rates)
- Leave-behind questionnaire
- Longitudinal design

SAGE: Current Biomarker Status

- Ongoing training
 - Understanding the collection process is important in the analysis process
 - Quality of collection determines what can be done
- Developing procedures to ensure comparability and quality
- Validation and revalidation of results
- Development of new assays



Developing New Assays: Challenges and Constraints

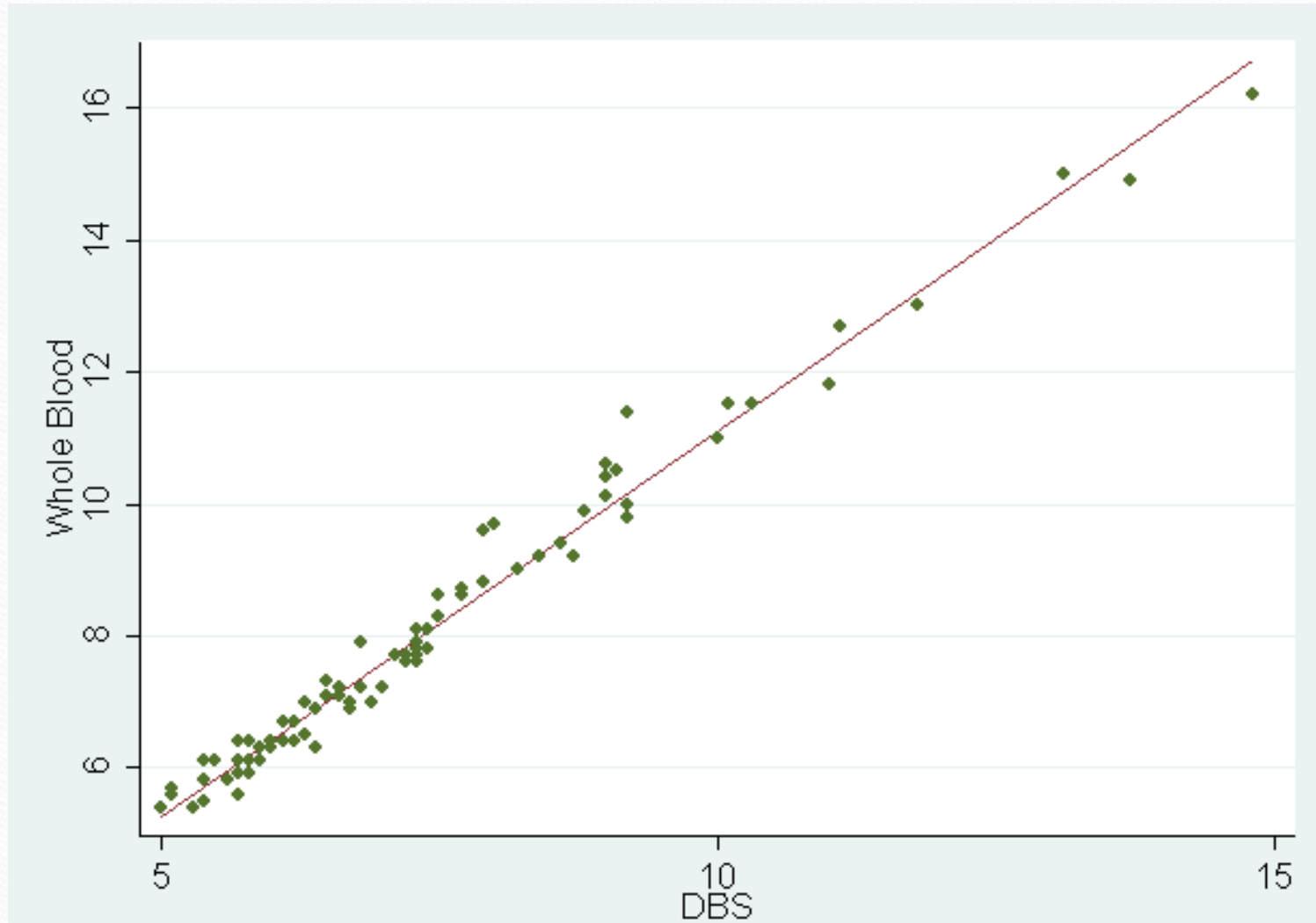
- Alteration of currently available kits is preferable for SAGE purposes
- Time and money are always an issue
 - Problems with serum/plasma assays are exacerbated with dried blood spots
- Evaluating priorities

HbA1c

- Measurement of glucose regulation
- Continues to glycosylate on filter paper when in contact with glucose
- Pretreatment necessary
- Attempt to maximize recovery from blood spots

HbA1c

$R^2 = .9877$



Previous validations: EBV and CRP

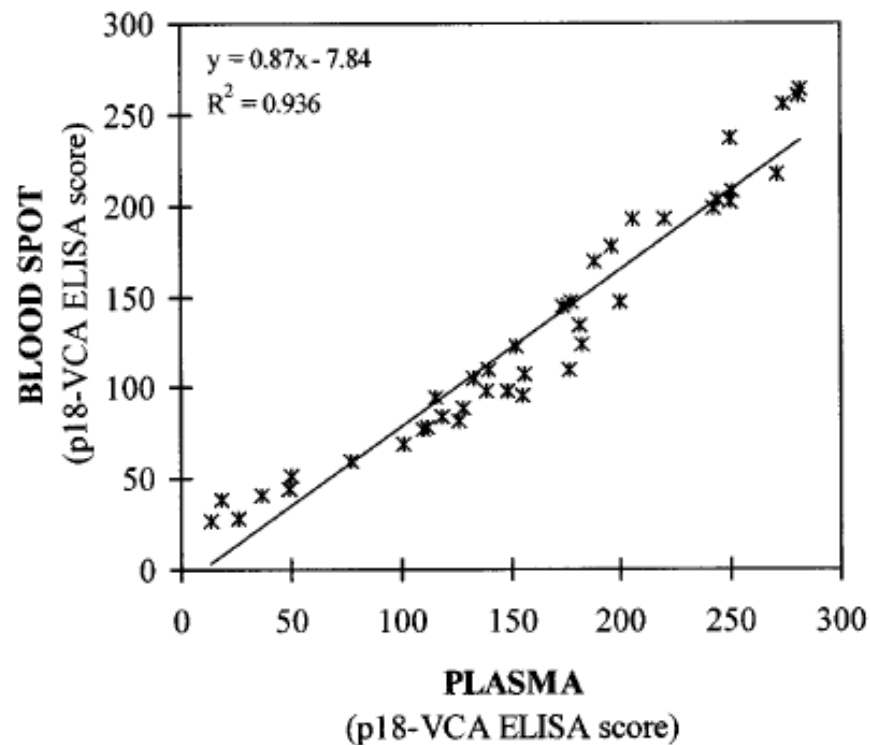


Fig. 1. Correlation between plasma and blood spot EBV p18-VCA antibody titer.

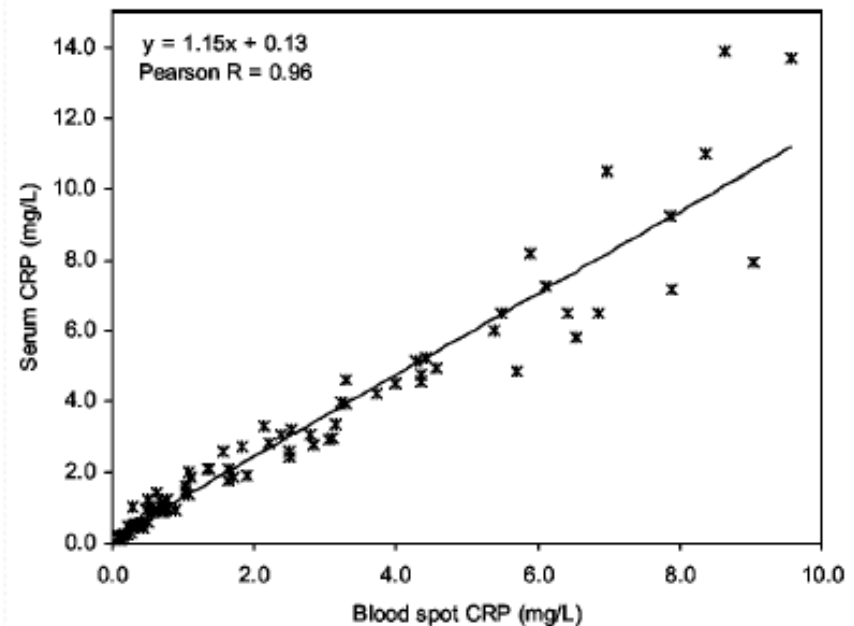


Fig. 1. Relationship between blood-spot and serum CRP concentrations in 84 paired samples.

Aknowledgments

- J. Josh Snodgrass, Department of Anthropology, University of Oregon
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