

**Joint Meeting**  
**ARC/NHMRC Research Network in Ageing Well**  
&  
**International Research Centre in Healthy Ageing and Longevity**  
**“Integrating the biomedical into psychosocial research on ageing”**  
**Melbourne, Monday 16 October 11:30am – 5:30pm**

**Meeting Notes**

**Workshop Participants**

<b>Local Researchers</b>	<b>Affiliation</b>	<b>Longitudinal Study</b>
A/ Prof. Emily Banks	National Centre for Epidemiology and Population Health, The Australian National University	The 45 and Up Study
Prof. Tony Broe	Scientific Director, Ageing Research Centre	Sydney Older Persons Study
Prof. Colette Browning	Monash Institute of Health Services Research, Monash University	Melbourne Longitudinal Studies on Healthy Ageing
Prof. Julie Byles	Director, Research Centre for Gender, Health and Ageing, University of Newcastle	Australian Longitudinal Study of Women’s Health
Prof. Leon Flicker	Prof. of Geriatric Medicine University of Western Australia	Perth Health in Men Study
Prof. Hal Kendig	ARC/NHMRC Research Network in Ageing Well	Melbourne Longitudinal Studies on Healthy Ageing
Prof. David Le Couteur	Centre for Education and Research on Ageing, University of Sydney	
Prof. Mary Luszcz	School of Psychology, and Centre for Ageing Studies School of Medicine, Flinders University	Australian Longitudinal Study of Ageing
A/ Prof. Gordon Lynch	Department of Physiology The University of Melbourne	
Prof. Mark Nelson	Head of General Practice School of Medicine, University of Tasmania	ASPREE Study

<b>International Researchers</b>	<b>Affiliation</b>
Dr Mitchell Harman	Director and President, Kronos Longevity Research Institute
Prof. Len Hayflick	Professor of Anatomy, School of Medicine, University of California,
Dr Donald Ingram	Acting Chief, Laboratory of Experimental Gerontology, Gerontology Research Center National Institute on Aging, National Institutes of Health, Baltimore
Dr James Joseph	Lead Scientist, Laboratory Chief, Laboratory of Neuroscience, Jean-Mayer USDA Human Nutrition Research Center on Aging, Tufts University
Prof. Jay Olshansky	School of Public Health, University of Illinois
Prof. Suresh Rattan	Danish Centre for Molecular Gerontology, University of Aarhus
Dr George Roth	CEO, GeroScience Inc Senior Guest Scientist, National Institute on Aging
Dr Bradley Willcox	Clinical Assistant Prof., Department of Geriatrics, John A. Burns School of Medicine, University of Hawaii
Assist. Prof. Craig Willcox	Okinawa Prefectural University-College of Nursing

<b>IRCHAL</b>	<b>Position</b>
John Weller	Director and ICHAL Conference Convenor
Noah Weller	Director and ICHAL Conference Co-Convenor

<b>Ageing Well Network</b>	<b>Position</b>
Dr Matthew Carroll	Senior Project Officer

### **Background Information:**

The joint workshop was an initiative of the Central Hub of the ARC/NHMRC Research Network in Ageing Well (Hal Kendig and Matthew Carroll) and the Network's Healthy Ageing Theme (Colette Browning) in collaboration with the International Research Centre for Healthy Ageing and Longevity (IRCHAL – John and Noah Weller).

The purpose of the day was to make a case for the inclusion of biological and imaging measures into psychosocial research in order to shed light and improve the experience of ageing as well. The other purpose of the day was to explore collaborations for cross-national studies which can give insight into regional differences in policy, population mixes etc.

### **Welcome and introductions:**

John Weller welcomed participants on behalf of IRCHAL and Hal Kendig on behalf of the Ageing Well Research Network. Participants introduced themselves and their research interests. Participants were asked to send more details on their specific interests to the Network for distribution to the group.

### **Invited presentations:**

#### **David Le Couteur – a clinical perspective on the uses of biological materials:**

From a clinical perspective ageing is complex and multifactorial so any interventions need to be multifactorial. The possible uses of biological materials include:

1. study of biomarkers e.g. albumin, renal function, telomere length etc
2. study of mechanisms of ageing – i.e. humans replace lab rats
3. study of disease risk factors
4. case-control studies of “successful ageing” vs. “frailty”

It is possible to collect blood, saliva, hair etc however blood is the most common type of collection. For example, participants in the Concord Health and Ageing in Men Project (CHAMP) have been willing to provide 100 mls of blood which is sufficient to conduct analyses on genes, hormones, cell lines and disease risk factors.

Disadvantages            Hard to get funding  
                                  Hard to locate qualified Australian referees for papers on the biology of ageing

Advantages                Logical approach to a complex problem  
                                  Requires novel solutions  
                                  Increased scope  
                                  Politically in favour

Additional data collection will lead to the generation of more hypotheses. However, in biology everything is associated and changes with age so there are many possible associations and it is hard to try and tease out causation and differentiate the effects of ageing from the effects of age-related diseases.

#### **Emily Banks - The collection of biological materials - followed by group discussion:**

Many studies already collect both biological and psychosocial data so it isn't a case of one versus the other. It is more about inclusion of both in order to get the complete picture on exposures, outcomes, confounding, interactions, prognostic factors etc.

Estimates of cost per person for blood sampling:

- Approximately 10 times that of survey data to cover collection, storage and retrieval
- Collection cost ranges from \$10 if using existing pathology service, \$50 if incorporated into a clinic visit with additional measures (can collect anthropometric and psychometric data at the same time)
- Storage, analysis and retrieval costs - \$50 minimum depending on intended use of sample – US studies suggest the total cost can be around \$1000 per person for more complicated analyses.

There may be issues to do with reduced participation rates when asking for consent for biological sampling, consent issues to do with conducting additional analyses outside the scope of the original study, and issues to do with the possible requirement for participant feedback on the outcomes of the analyses.

Other sampling options:

- Buccal smears – only provides information on genetics so less useful than blood. Methods in genomic research are improving so sampling requirements will reduce over time. Can be used as a graduated approach – if not willing to give blood may be willing to provide a buccal smear.
- A self-administered and mailed-in Guthrie pin prick test can be a cheap alternative to clinic-based blood sampling.
- Skin biopsies can be powerful as over 100 skin lines can be grown but it is expensive and time consuming and there may be difficulties in obtaining them from very old people. The Baltimore Longitudinal Study of Aging (BLSA) have published on longitudinal changes in telomere length and have made their tissue cultures available to external researchers.
- Post-mortem tissue – have been done in Hawaiian study and in the later stages of the Sydney Older Persons Study (SOPS).
- Less expensive cognitive measures like reaction time, memory or physiological measures like grip strength may be cheaper alternatives when funding for blood or imaging is not available.

### **Tony Broe - Imaging information – followed by group discussion:**

The ageing brain is a patchwork of changes that imaging techniques can monitor. Imaging is an important measure that should be included in psychosocial studies because of the links between brain development and the fact that neurodegenerative disease will become increasingly important as the prevalence of other forms of disease such as infections and cardiovascular disease declines. Imaging data has the potential to act as biomarkers to:

- differentiate “normal” ageing from selective, potentially preventable processes or “diseases”;
- define predictive factors for “normal” brain ageing;
- define the natural history of brain disorders;
- define predictive factors for brain diseases; and
- direct better use of neuroprotective agents.

Imaging techniques and possible uses:

- Volumetric MRI – T1 – monitor Alzheimer’s disease, amnesic mild cognitive impairment (MCI), and memory in “normal” ageing as well as monitoring neural structure and volume
- FLAIR and T2 – monitor white matter abnormalities, pathways, linkages
- Cortical thickness – confirms the above volumetric findings and may identify new areas of loss and pattern of age-related changes. A longitudinal study of cortical thickness changes would be invaluable.
- Transcranial sonography – may be a biomarker of motor impairment including Lewy Body Diseases such as Parkinson’s and pre-Parkinson’s Disease
- Imaging can also be incorporated into functional studies using functional MRI or PET and studies of biological agents like dopamine.
- Can be used to monitor changes longitudinally such as neural development and decline.

As well as being able to monitor the above changes, imaging data has the advantage of not having storage issues as the information can be digitally stored and shared internationally. There are, however, a number of disadvantages:

- Costly – one hour is long enough to take all the above measures (except MRIs) but costs \$650 (this will decrease over time as will the mobility of the machines)
- Technological changes mean machines are regularly updated so it is hard to obtain consistent measures over time.
- Requires a high level of analytical expertise
- Consent can be an issue as can tolerance as the process is noisy

Existing examples of combining imaging and psychosocial research:

- Denmark study combining functional cognitive measures plus blood, physiology etc
- NIA longitudinal ageing studies with muscle MRIs, brain imaging, PET scans etc - very expensive
- Gary Smalls at UCLA
- Researchers at the University of Michigan are doing functional MRIs on a subset
- PATH study at ANU doing imaging on a subset (info to be distributed to all later)

### **Suresh Rattan – The biology of ageing:**

Ageing is a biological issue at all levels and everything else is a manifestation of that basic process. We have learned a lot and the major picture is now drawn. However, ageing is individualistic, even at a molecular level, and more information is needed on the variants, especially in older people. For example, a huge European study of zinc found that different countries have different genotypes and different zinc requirements in their diets.

Each study should have a program of work including cross-sectional, longitudinal, interventions and so on because converging evidence from different directions is needed to attempt to evaluate causality. Meta analysis offers a useful approach across projects.

### **Colette Browning - What is “Healthy Ageing” and what determines it?:**

The definitions of “healthy ageing” are often circular and the main models focus on physical activity. It is easy to see the effect of these activities but they are hard to sustain over time. Models are poor on predicting this maintenance of behaviour change.

A key question to consider is how can one take basic biological knowledge and interrelate it with action to increase motivation and monitor outcomes? A successful approach will require the education of the target population and changes to the environment that will promote the desired healthy behaviours.

There are many conflicting messages released to the public so we need to make sure that all messages are grounded in replicated broadly based empirical data.

## **Discussion Summary**

### **Methodological issues:**

#### **1) Selecting from a subsample rather than the entire cohort.**

It can be more cost-efficient to collect from a subset of the cohort using a nested case-control or case-cohort design. It can also be a benefit to collect materials at a later point in the process once the project is underway and funds can be sourced. Samples can be taken over time in order to monitor changes longitudinally.

#### **2) How to strategically select a subsample for biological sampling?**

- If testing a specific hypothesis - a clinical examination is required on all and then select a subset based on set of criteria determined by the hypothesis – i.e. gender, age, exposure etc.
- If many hypotheses or none set yet – a random sub-sample (case-cohort) is a versatile approach as selecting based on particular exposures will limit future use of the resource.

#### **3) Number of samples required?**

The UK Biobank power calculations suggest that 500,000 samples. However a few samples can be enough to give predictive power – e.g. 150 samples covering all genotypes. A staged approach is efficient starting with a few to see if there is a relationship and then do more to get the definitive result.

#### **4) Integrating existing datasets:**

There is an international movement towards integrating existing datasets in order to increase the power and generalisability of the resultant combined dataset. The following examples were discussed:

Ageing specific collaborations:

- Centenarian data (a meeting in Korea was scheduled just after the date of this workshop)
- The National Institute on Aging (NIA) in the US has set up the “Publicly Available Database of Aging-Related Secondary Analyses in the Behavioral and Social Sciences” (including the Australian Longitudinal Study of Ageing) and is developing protocols for combining datasets
- The DYNOPTA project which will combine nine Australian longitudinal studies of ageing

Non-ageing examples that may provide valuable advice on the process of integration, standardising measures etc:

- Human Genome Project – calling for the use of standard measures to facilitate later integration
- Oxford “Collaborative Group on Hormonal Factors in Breast Cancer”

A critical issue with the attempt to integrate datasets is the use of different outcome measures making it hard to combine the data. There may also issues to do with social and cultural biases in the datasets, differences in interview techniques and issues to do with the reliability of the data. This sort of collaboration is far more challenging than integrating biological data.

**Action** – The Network will put out a call to existing Australian studies to see how many centenarians they have and the possibilities of combining the data. The outcomes of this call will be sent to meeting participants.

### **The search for biomarkers of ageing:**

Biologists are enamoured with biomarkers and the possibility of changing the ageing process. They think they measure ageing at a fundamental level, like telomere length, but these measures are generally only correlated with chronological age and there is no evidence of any long-term predictive value.

Predictors of longevity, morbidity, future function are much sought after. Psychosocial research fares better than biology in terms of measuring disability and function so psychosocial measures could be incorporated in the analysis. A battery of biomarkers will be required rather than a single measure as it is an interaction of many systems which would change together to predict ageing. To integrate these measures would need large numbers in order to have the statistical power.

### **Gene - Environment approach:**

A popular approach is to try to identify genetic and/or personal/family histories that predispose people to disease or lifestyles so that we can tailor treatments to the individual. In reality this is generally not possible as the gene-environments are too complex at an individual level. We can find usually only find general risk factors for the group.

### **Tissue banks:**

There are existing disease specific tissue banks which have medical records and so on but to make use of this for epidemiological research would require the inclusion of control subjects and the collection of additional psychosocial data on the banked subjects. It would be better to incorporate a tissue bank into an epidemiological study and request tissue consent from the start because too many participants may die or refuse consent in later waves.

There are many different biological hypotheses in ageing that can be tested using tissue samples so most research tends to take the simpler disease perspective. Need a national resource to do set series of measures, the outcomes of which would be publicly available along with the tissue – a centralised resource. Powerful hypotheses dealing with the following areas are needed to champion this development:

Ageing

Disease studies – good to capture funding

Cell culture – including telomere length, serum

Serum analyses suggest that multiple factors give protection against age-related declines but this has not been validated long-term. Information on lifestyle, personality type, stress etc (or allostatic load as the base concept) would be valuable. An Australian study on carers of Alzheimer's patients linking allostatic load, stressors, lifestyle, and biology is an example of this type of research.

There are no powerful biomarkers of allostatic load but skin biopsies can be used to test stress responses however this is very labour intensive. This situation will improve once microarray gene profiling becomes reliable – could be used as static measures or in response to stress.

### **Funding strategies:**

A big data vehicle should be developed which is cost-effective to run new comparisons or add new measures to the battery. Infrastructure funding could be obtained to build the resource and once built this could be used as a platform to get project/program funding to do specific analyses.

Many studies already have materials in storage that could be utilised for new analyses so an argument to the NHMRC or other funders needs to be developed to provide the funds to be able to utilise this material.

A combination of funding strategies (enabling and infrastructure grants and perhaps corporate funding) and taking advantage of current hot topics will be required to build the resource. Once built, materials should be provided to researchers on a cost-recovery basis in order to maintain the resource.

### **The need for a cross-sector approach – possible arguments to facilitate change**

Knowledge and is generally compartmentalised by discipline, industry, and political sector and this can impede action. One argument that brings the sectors together is the fact that that poor health in late middle age is a key factor for early retirement so healthy ageing is critical to increased workforce participation.

The ICHAL Top Ten Tips developed at the ICHAL conference (see attachment 1) could be reframed to combine a personal, community and national perspective showing how what is good for the individual is also good for the country. This would fit into Australia's national goal of an 10 years of additional productive ageing.

Jay Olshansky outlined the "Longevity Dividend" which argues that if we can increase longevity by 7 years we will reduce the age-specific risk of all diseases by half and increase working life (see attachment 2 - Olshansky et al., 2006 – attached separately). The implications of this argument are currently being assessed by economists in the US and could be a powerful argument to use in the Australian Policy setting.

### **Possible IRCHAL initiatives**

**Wet Lab** - The possibility of IRCHAL setting up a wet lab was discussed. The wet lab proposal was seen as strongly dependant upon funding and several of IRCHAL's International Advisory Council members that were present indicated that they would like at IRCHAL's headquarters a storage facility for Cell and biological material samples, and in the future facilities for joint research projects. Len Hayflick showed particular interest in the discussion on a Cell and biological material repository and said that an inventory of Australian samples could lead to valuable research projects on the biology of ageing.

**IRCHAL Base** - John Weller indicated IRCHAL is keen to establish a physical base to enable enhanced collaboration between the international researchers who are members of IRCHAL with Australian researchers and students. It was IRCHAL's desire to set up workshop/educational facilities to house both national and international seminars and high powered think tanks.

**IRCHAL Fellowship** - the possibility of setting up a fellowship including covering the cost of consumables was also discussed.

### **Research possibilities**

#### **1) Imaging studies**

- a. Could look at positive protective factors e.g. can lose or gain thickness with age. Could look at children and follow hippocampal growth – would be valuable opportunity to have a life study looking forward and feeding into what we currently know about ageing
- b. Could compare centenarians with younger old people with Alzheimer's

**2) Aboriginal research** - examine at the relationship between educational deprivation and cognitive activity in aboriginal people. Aboriginals show premature geriatric syndromes as they have an earlier onset of diseases. Those that survive beyond 65 have similar longevity to the rest of the population – a survivor effect. The 45 and Up Study first round had 1% of respondents in the first round of 36,000 people who identified themselves as aboriginals so they expect 2,500 to be in the final sample. Multiple studies are already planning to do research on this group.

**3) Alternative therapies** – a comparison of the treatment effect of yoga and drugs or look at alternative therapies as an interface between biological and psychosocial.

**4) Biomarkers of ageing** - examine the modifying effect of physical and cognitive activity or nutrition. Studies have shown an increase in function in response to these factors but there is no information on the biological factors mediating this effect. Could develop an argument to request additional funding for existing or new studies to collect biological materials.

### **Proposed Directions:**

- 1) Consider proposals for research funding where there is genuine added value – e.g. adding an Australian component to an international indigenous ageing study or a local study focusing on key local factors that add to knowledge – e.g. skin cancer, ageing and sun exposure.
- 2) Develop strategies on how to better link biopsychosocial data and promote future collection including conducting an audit of centenarians in existing Australian studies.
- 3) IRCHAL lab options to be considered
  - a. Set up a wet lab?
  - b. Sponsoring key visitors from overseas to spread knowledge, techniques and directions – should be the key people actually conducting the research rather than the lab heads.

- c. Central store for biological material so samples from multiple studies are brought together to save money through economies of scale. Samples can then be provided to labs with specific analytic expertise.
  - d. Virtual lab – get labs to collaborate and identify the key topics and assign to the lab best able to do the analysis.
- 4) Facilitate local and international collaborations on grant applications – Matthew to request international participants to identify their analytical capacity and research interests.
  - 5) Build infrastructure to link biological materials and individual histories – e.g. tissue bank plus a personal minimum dataset – we will investigate the international association of cell banks and do an inventory of Australian biological sample banks and what personal data they hold, what the access and consent requirements are, what biopsychosocial outcomes have arisen etc.
  - 6) Develop conceptual ideas on linking biological and psychosocial, e.g.:
    - a. Stress/allostatic load
    - b. Gene-environment interactions for specific groups.
  - 7) The Ageing Well Network could run seminars on the biopsychosocial aspects of ageing or produce a discussion paper as per the Network's translation mission.
  - 8) Develop cross-sectoral arguments for funding and policy change.
  - 9) Local members to continue meet between now in order to further these discussions prior to the next full group meeting at the next ICHAL conference. Additional key Australian researchers unable to attend the workshop will be included in these ongoing discussions.

#### **Closing discussion:**

John Weller said that when information was at hand regarding the integrating of existing data, a strong application for funding should be made to the Australian Federal Government for storage/wet lab/education facilities to enable a strong growth in national and international research.

Colette Browning, Noah and John Weller and Hal Kendig thanked the participants for contributing to a vigorous discussion and being willing to continue to work together to progress the ideas discussed. A meeting could be sought with the relevant Ministers from the Australian Government to discuss future support and directions.

# Attachment 1: ICHAL Top 10 Tips



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"The mission of the International Research Centre for Healthy Ageing & Longevity (IRCHAL) is to promote healthy ageing & longevity through interdisciplinary collaboration amongst the world's leading experts on the science of health, ageing and longevity, and to disseminate evidence-based knowledge throughout the nations of the developed and developing world for the betterment of humankind."





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HEALTHY AGEING  
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IRCHAL collaborates with "the who's who" of leading international experts from throughout the world from a broad array of disciplines relating to health, ageing and longevity to create harmony and the exchange of knowledge between the various disciplines in order to address the challenges and opportunities of an ageing society. With its international advisory council of leading experts, IRCHAL occupies a unique niche in the world of biogerontology, social gerontology, and clinical geriatrics.

**United Nations  
Programme on Ageing**

IRCHAL works in consultation with the United Nations Programme on Ageing and supports its efforts towards implementation of the Madrid International Plan of Action on Ageing.

3rd International Conference on Healthy Ageing and Longevity  
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**3RD INTERNATIONAL CONFERENCE ON  
HEALTHY AGEING  
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Melbourne | October 13th 14th 15th  
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Sunday 15<sup>th</sup> October 2006  
**Plenary Panel Discussion:  
IRCHAL's Top 10 Tips  
for Healthy Ageing &  
Longevity**  
from a Panel of Leading Experts




### IRCHAL Panel of Leading Experts:

Dr. James Joseph, JM-USDA Human Nutrition Research Center on Aging, Tufts University, USA.  
Prof. Suresh Rattan, Danish Centre for Molecular Gerontology, University of Aarhus, Denmark.  
Dr. Donald Ingram, National Institute on Aging, National Institutes of Health, USA.  
Prof. Colette Browning, Monash University, Australia.  
Dr. S. Mitchell Harman, Director & President, Kronos Longevity Research Institute, USA.  
Prof. Hal Kendig, ARC/NHMRC Research Network in Ageing Well, University of Sydney, Australia.  
Prof. S. Jay Olshansky, University of Illinois at Chicago, USA.  
Prof. Helen Bartlett, Australasian Centre on Ageing, University of Queensland, Australia.  
Prof. Leonard Hayflick, University of California, San Francisco, USA.  
Dr. George Roth, Senior Guest Scientist, National Institute on Aging, USA.  
Prof. Leon Flicker, University of Western Australia and Royal Perth Hospital Australia.  
Dr. Reubin Andres, Clinical Director, National Institute on Aging, National Institutes of Health, USA.  
Prof. Julie Byles, University of Newcastle, Australia.  
Dr. D. Craig Willcox, Okinawa Prefectural University College of Nursing, Japan.  
Dr. Bradley J. Willcox, Pacific Health Research Institute and the University of Hawaii, USA.  
Mr. Noah J. Weller, International Research Centre for Healthy Ageing and Longevity (IRCHAL).



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1. Have Good Genes ("Choose your Parents Wisely!") – Be Lucky
2. Be in Control – Shape your Own Future/Your Own Old Age!
  - Empower yourself to take responsibility for your own health
  - Modify your behaviours (healthy diet, exercise, healthy weight, don't smoke, drink in moderation, reduce financial debt)
  - Modify your environment (built, social, economic)
  - NB: We need public health programmes that get people to actually do the above
3. Have Positive & Meaningful Personal relationships
4. Have Goals in Life (especially in retirement)
  - This will get you out of bed each morning (contribute to society via work, charity, volunteer work)
5. Have access to good healthcare
  - Prevent, detect early and manage age-associated disease



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6. Population Strategies: Remove the threats to Public Health
  - Equality in Society, Optimal Nutrition, decrease Obesity, increase Physical Activity, aim for Economic Security for all.
  - Life-Course Approach to Healthy Ageing – don't wait until it is too late
  - Invest in more & more and & more research!
  - Create harmony and improve dialogue between the scientific community, the medical community, allied and complementary healthcare professionals, and the public.
  - Bridge the gap between Scientific Knowledge & Traditional Knowledge. Have more conferences like the International Conferences on Healthy Ageing & Longevity.
7. Adaptation
  - Adapt in positive ways to all of the changes that an ageing body inevitably brings forth (Be "homeotic")
8. Avoid extremes in your life (Diet, Personality, Psychological/Spiritual, Physical Activity, avoid conflict)
  - Health & Longevity is about BALANCE!
9. Never Give Up Your Quest for (evidence-based) Knowledge
  - But don't be a Sucker! (And NEVER buy hormones on the internet!)
10. Ageing is a privilege – Please enjoy and embrace the experience of the transitions to each stage of life



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Please send comments/feedback to:

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