**Cohort Profile: The Kiang West Longitudinal Population Study (KWLPS) – a platform for integrated research and health care provision in rural Gambia.**

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**Profile in a nutshell**

* The Kiang West Longitudinal Population Study (KWLPS) is a prospective cohort, served by the MRC Keneba field station (MRC Unit, The Gambia); it supports research particularly in nutrition, infection and growth.
* KWLPS is located in rural Gambia and started with the collection of longitudinal multi-generational data for four ‘core’ villages going back to 1950. It was more recently expanded to include all residents in the Kiang West District (all ages, N>14,000 across 36 villages), enabled by the introduction of linked database systems and platforms: The Kiang West Demographic Surveillance System (KWDSS since 2004), the Keneba Electronic Medical Records System (KEMReS since 2009) and the Keneba Biobank (since 2012).
* Follow-up for KWDSS is 3-monthly and forms the sampling frame for all ongoing and future data collections within the KWLPS.
* KWLPS comprises a wealth of demographic and phenotypic measures, genetic and epigenetic data and biological samples, facilitating the integration of research and health care provision to the whole of the population.
* Data access is managed via the MRC International Nutrition Group (www.ing.mrc.ac.uk).

**Why was the cohort set up?**

Research on malnutrition and malaria has been conducted in the Kiang West (KW) district of The Gambia (West Africa) since 1950, initially through Professor Sir Ian McGregor’s annual anthropometric and health surveys of the rural subsistence farming community in this low- and middle-income country (LMIC) setting (described in more detail in1). With the establishment of a permanent field station by the UK Medical Research Council (MRC Keneba) in 1974, research and health provision expanded into the wider community. MRC Keneba is located in the heart of the 750km2 district located in the Lower River Region, which until 2014 had limited road access (Figure 1). Research facilities in KW were initially set up to support nutrition studies in particular for longitudinal studies of growth in four ‘core villages’ (with ~4000 residents). Since 1989 research studies also recruited participants from the wider district. The establishment of the comprehensive demographic surveillance (Kiang West Demographic Surveillance System (KWDSS)), electronic medical record (Keneba Electronic Medical Records System (KEMReS) and biobanking platforms (Keneba Biobank) now comprises an integrated system for research and health care provision to the whole of the Kiang West Longitudinal Population Study (KWLPS) cohort (N~14000 across 36 villages).

Since 1949 this work has primarily been supported by funds from the UK Medical Research Council (MRC) and the UK Department for International Development (DFID) under the MRC/DFID Concordat agreement to the MRC International Nutrition Group (current grants are MC-A760-5QX00, U105960371 and U123261351).

**Who is in the cohort?**

The population of Kiang West is predominantly of Mandinka ethnicity (Mandinka 79.9%, Fula 16.2%, Jola 2.4%, other 1.3%) living across some 36 villages. Villages are divided into compounds, where extended multi-generational families live together, with an average of 16 people per compound (range 1-170). This predominantly Muslim society practises polygamy. Rural subsistence farming is the main livelihood. Income and eating patterns fluctuate strongly according to the annual farming calendar, heavily influenced by the monomodal annual rainy season (June to October). Although more than half of the Gambian adult population has not received any education, with higher proportions in rural areas, the gross enrolment ratios for lower basic (7-12y) and upper basic (13-15y) education are around 88% and 66% respectively, with an increase in the number of girls attending school over the years; approximately half of the children not in lower basic education attend Islamic schooling2,3.

The ‘core’ villages of Keneba, Manduar and Kantong Kunda and for a limited period Jali, have been the subject of longitudinal demographic and health surveys since 1950. In 1974 and 1977 regular outpatient and antenatal clinics were established, respectively, in Keneba to serve the medical needs of these villages. Healthcare provision and research studies after 1989 started to extend beyond the core villages in the wider Kiang West District (Figure 2). Since 2004 all Kiang West residents are captured by the KWDSS, this now forms the backbone of the data flow structure and participant recruitment for all MRC research studies in the region (Figure 3). In 2009 the KEMReS was launched to capture detailed morbidity data of Kiang West citizens for all primary health care contacts with the clinic at MRC Keneba. The Keneba Biobank was established in 2012. All recent and ongoing research projects are linked to one or more elements of the platforms triad KWDSS/KEMReS/Keneba Biobank. Data capture using electronic tablets has been introduced for our most recent studies in the region. Study-specific databases are not described here in detail, but we refer the reader to the references in the findings section below and our publication list via the MRC ING website ([www.ing.mrc.ac.uk](http://www.ing.mrc.ac.uk/publications.aspx)). However, information on longitudinal databases (i.e. core village and other longitudinal data), as well as systematically collected data, is given in the following sections. Summary statistics for the Kiang West Longitudinal Population Study cohort are shown in Table 1 and Supplementary Figure 1.

**How often have they been followed up?**

***Core village and historic data*** The conduct and content of demographic and health surveys, clinics, vaccination programmes prior to 2004, as well as the resulting reduction in mortality have been described in detail by Rayco-Solon and colleagues 1. Medical data at the MRC Keneba clinic were collected on paper prior to 2009. Data of structured child welfare clinics, vaccinations and antenatal clinics were entered into a database for those residing in the core villages since around 2000 (Figure 2). The remainder of medical data recordings for Kiang West residents beyond the core villages was not electronically transcribed prior to 2009.

***KWDSS*** The main purpose of the KWDSS is to provide reliable and up-to-date demographic data on the population of the KW district to support the many research projects conducted by MRC in the district. In particular it provides:

1. A common numbering system for all Kiang West residents and study subjects;
2. Accurate dates of birth and identification of parents;
3. Sampling frame for study subject selection;
4. Population structure, used to facilitate the design/assess feasibility of new studies;
5. Residence histories for survival analyses;
6. Tracking of individuals’ movements to facilitate longitudinal and follow-up studies.

Every individual who has been resident in Kiang West since 2004 and all who have taken part in our studies before that date, are assigned a unique ID, the West Kiang number (WKNO). Every compound in the district is visited once every 3 months according to a fixed schedule. The first two months of each cycle are dedicated to routine visits while the third is set aside to resolve discrepancies and double registrations, link the unique ID of the parents of newly registered individuals, linking district-internal migration movements and conduct quality assurance. At each visit a senior member of the compound is interviewed to provide the required information.

Since the KWDSS is used as a sampling frame within the KWLPS, maintaining the integrity of the linkages within the KWDSS, and between it and other databases is critical. In order to achieve this we impose two basic constraints: (a) no individual can be recruited by a study or the clinic until they have been assigned a unique ID number and (b) no delivery can be recorded in the maternity database unless the mother has an “open” pregnancy episode recorded. It is also often necessary to find the unique ID number of an individual based on limited information, but this is not always a straightforward task in a setting such as rural Gambia. For this purpose we devised a search utility, the ‘Demography Search using Bayes’ (DSUB) algorithm to search the KWDSS database for individual(s). The user may input whatever is known of the individual, the programme outputs the best matches. The KWDSS is a registered INDEPTH Network (http://www.indepth-network.org/) member centre. Additional information on the KWDSS including the search algorithm programme is given in the Supplementary Materials.

***KEMReS*** The primary health care clinic at the MRC Keneba field station (Figure 1) provides general health care to all Kiang West citizens who present with acute or chronic medical conditions. Around 1500 patients, excluding visitors to Kiang West, are seen each month with seasonal variation (Supplementary Figure 2). Children under 5y attend the clinic in Keneba about four times per year depending on the village of origin within the district and transport availability. Emergency presentations are seen 24h per day. General, child welfare, antenatal/postnatal and non-communicable disease (NCD) clinics are run weekly. An observation room allows stabilisation of patients, but full inpatient facilities are not available. Patients requiring treatment at a secondary/tertiary medical facility get transported to either the clinic at MRC Fajara or the Edward Francis Small Teaching Hospital (formerly the Royal Victoria Teaching Hospital) in Banjul, both 2-3h by road.

KEMReS started recording patient attendances in December 2009 and was designed to capture clinical data of all presentations at the clinic at MRC Keneba across all age groups, to understand in depth the epidemiology of communicable and non-communicable diseases, to support on-going research projects and to improve clinical care for the population. The database also incorporates data on regular child welfare clinics (<2y) and vaccinations. Electronic capture of antenatal/postnatal information was added to KEMReS in 2013. KEMReS as a platform in conjunction with the other databases can provide details on adverse events and/or morbidity data as outcome measures for clinical trials in the district. For more detail on the KEMReS set-up access see Supplementary Materials.

***Keneba Biobank***The Keneba Biobank was initiated in May 2012, as a platform for genetic studies and the collection of biological samples and simple phenotypic measures for all consenting individuals captured by the KWDSS. A custom-designed database and sample tracking system was introduced, which is used for all Biobank-related processes. The Keneba Biobank is currently in its first round, with recruitment standing at >9000 participants to date. To ensure an even distribution of recruitment by season, the region was block randomised into 10 sectors of roughly equal size comprising either a single village or several smaller villages. Every two weeks, recruitment moves to a different sector, with all sampling and most measures conducted in the field. Participants are visited in the early morning to obtain age-group specific data and (fasted) biological samples. Clinical referral criteria were defined to identify urgent referrals (malaria or severe high blood pressure) observed during the field visit. Affected participants, as well as those who report feeling sick, are brought back to the MRC Keneba clinic on the same day for evaluation by a clinician. Non-urgent referrals (high glucose level, high blood pressure, anemia) are identified via a search function within the Keneba Biobank database, and cases are called within a few days for retesting and clinical evaluation during regular clinics (e.g. the weekly NCD clinic).

The Keneba Biobank is part of the LMIC Biobank and Cohort Network (BCNet, <http://bcnet.iarc.fr/>)4. Additional information on the Keneba Biobank is given in the Supplementary Materials.

**What has been measured?**

***Core village and historic data*** The KWLPS database comprises computerised records of all Kiang West residents (N~14000). For core village residents (N~4000) these date back to 19501, representing life-course longitudinal nutritional and health phenotypes, particularly relating to anthropometry/growth and maternal health. The consistent and longitudinal recording of the following measures were introduced over time:

* Since 1949: Exact date of birth and parents’ IDs;
* Since 1980: Birth (weight, length, gestational age, delivery date); growth (weight, height, mid-upper arm circumference, head circumference) for children on up to 12 occasions before 2y of age and less frequently thereafter); demographics (parents’ IDs), pregnancy outcomes and reproductive histories; records of self-referrals to clinic; outcome measures from numerous specific studies;
* Since 1990: Most studies include anthropometric measurements, blood pressure, dietary and lifestyle information, blood and urine samples. In selected study groups detailed data on bone mineral content and density, bone dimensions and more recently bone age, and muscle force and power has been measured.
* Since 1996: Vaccinations

Please note that details of study databases are not described here, further information can be found in the findings section below and via the MRC ING publication list ([www.ing.mrc.ac.uk](http://www.ing.mrc.ac.uk)).

***KWDSS*** During each KWDSS round the following information is captured: migration movements into and out from the compound (both internal and external including contact details for those leaving the district), births and deaths, pregnancies (to avoid missing infants who die during the neonatal period), marriages and the names or unique ID of the parents of all new-borns or new arrivals. Details of husbands of married women are mostly recorded to identify the children’s fathers. All changes in status for each Kiang West citizen are captured.

An important feature of the KWDSS is that we allow data to be recorded from other sources. For instance, births and pregnancies may be derived from the maternity arm of KEMReS. Similarly, information is rectified when patients present to the general Keneba clinic. This ensures that dates of birth are recorded accurately and up-to-date data on individuals is available from a single database table without needing to wait for the next KWDSS round. The two main types of data tables used by KWDSS are “constant” and “episode” (for details see Supplementary Materials). Briefly, constant tables are mostly used to record unchanging data such as name or date of birth. Episode tables record details of time intervals, e.g. the residency of an individual living in a particular compound.

***KEMReS*** KEMReS records a set of data entry fields for each stage during a patient encounter based on well-known clinical examination routines (Supplementary Figure 3, Table 2)5. Recorded information includes data on anthropometry, vital signs, symptom history and examination findings, laboratory investigations, diagnoses and prescriptions provided. Data is stored with two specified ranges according to age: (1) Normal range (2) Possible range. An alert for the clinician/nurses appears for values out of the normal range to address the finding clinically. A full data set at each stage needs to be entered before the patient can proceed. This ensures the accuracy and completeness of data collected at each clinic visit.

Past encounters and medical history are stored and updated with each patient encounter to aid clinical assessments and medical decisions. Diagnoses are recorded using the WHO ICD-10 coding system6. Diagnoses also include ‘Well with a complaint’, ‘Well without a complaint’ and ‘Unknown diagnosis’. A free text entry can be used to describe possible diagnoses further. KEMReS is not a clinical decision support system although this can relatively easily be added. However, KEMReS consists of a number of user interfaces with several functionalities including clinical care reports, referral letters, management reports and medication dispensary reports. Furthermore alerts are set for due vaccinations and drug prescriptions to be in line with international guidelines on patient management7.

***Keneba Biobank*** Table 4 shows a summary of data and samples collected as part of the Keneba Biobank by trained staff using standardised operating procedures. Briefly, age-group specific data and samples collected comprise: biological samples (venous blood, urine); questionnaire; anthropometry, body composition based on bioelectrical impedance (using population-specific equations8), and blood pressure. Biological sample processing and a limited number of analytical tests are conducted on fresh specimens at MRC Keneba. Analytical tests conducted comprise fasting glucose, malaria, zinc protoporphyrin (discontinued in 2014), and full blood count. Samples processing involves the separation of blood fractions (serum, plasma, washed red blood cells), treatment of urine and DNA extraction; all samples are split into several aliquots and stored in 2D-barcoded microtubes at -70°C within 2-4hr of collection.

Ethical considerations

All studies and data collections in Kiang West are presented to and approved by the MRC Unit The Gambia Scientific Committee (SCC) and joint Gambian Government/MRC Unit The Gambia Ethics committee, which is overseen by the ethics board of the London School of Hygiene and Tropical Medicine (LSHTM). For research studies all participants and/or legal guardians provide written, informed consent.

**What has it found? Key findings and publications**

Summary statistics of the KWLPS compared to national data from The Gambia are shown in Table 1. It is noteworthy that, mortality rates have improved dramatically over the last decades1 with higher life expectancy in women and greater reductions in crude and child mortality rates seen in KW than elsewhere in The Gambia2,9. Differences are likely due to higher standards of clinical services children and women receive, including regular child welfare clinics and ante- and post-natal follow-up in KW, compared to other regions. Slightly higher neonatal, post neonatal and infant mortality rates in KW compared to national data probably relate to the better capture of data on deaths, since almost all pregnancies are monitored and their outcomes recorded. Table 3 shows the 10 most common medical diagnoses by age group based on ICD-10 coding6. Morbidity patterns are similar to previous studies in the sub region with around 30% related to respiratory illness10. In those over 50y old, NCDs form a large part of clinic presentations. Prevalence of malaria across the whole of the Gambian population has decreased recently11 and particularly in those under 10y malaria presents now fewer than 2% of all clinic presentations.

There are numerous publications describing the vast body of research conducted in the KWLPS since the early 1950s, too many to list and describe. However, the key findings and publications can be broadly described under the categories of i) secular trends, ii) major research findings and iii) recent developments. A short summary of these is given below, for a comprehensive list of references over recent years see our publication list via the MRC ING website ([www.ing.mrc.ac.uk)](http://www.ing.mrc.ac.uk)).

i)Reports on secular trends describe declining mortality trends1,12,13, intergenerational and demographic transition effects on growth14,15 and survival16; reductions in diarrhoea rates17, declining malaria rates11.

ii) Major research findings include: Insights into season of birth or conception effects on mortality18, immune outcomes19, and DNA methylation20; effects of pregnancy supplementation on low birth weight21; increased understanding of growth faltering and identification of critical windows beyond the ‘first 1000 days’ for possible nutritional interventions to address stunting22; lack of anticipated benefits of calcium supplementation in children and pregnant mothers consuming a very low calcium intake, with identification of unexpected, possibly adverse, long-term skeletal effects23–25; the use of MUAC to identify infants at increased risk of death in LMIC26 and the efficacy of hepatitis B vaccination after 24 years of follow-up27.

iii) More recent developments with respect to the KWLPC are covered by the following publications on: Early nutrition and immune development via a birth cohort followed-up since 2010 (the ENID trial)28; life course nutrition and health, including immune/inflammatory outcomes29 and cognitive development30; and the role of the iron-hepcidin axis in infection31,32; and seasonal effects on blood cell composition33.

**What are the main strengths and weaknesses?**

**Strengths**

* Stable, well-characterised and ‘research friendly’ population in rural Sub-Saharan Africa of high homogeneous ethnicity. Exceptional long-term relationship between population and MRC maintained through high levels of communication between MRC staff and villages and with great care taken to ensure research ethics.
* Computerised records of all KW residents, some of which date back to 1950, representing a unique level of life-course nutritional and health phenotypes including: birth anthropometry and details of mother's health and nutritional status in pregnancy; detailed serial post-natal anthropometry; active health surveillance at child welfare clinics from 0-24 months; records of self-referrals to clinic thereafter; reproductive histories; outcome measures from numerous specific studies.
* A setting that facilitates research on the complex relationships between diet, health and survival in an environment where infectious diseases still play a major role in mediating population health, e.g. seasonal influences.
* Integrated demographic surveillance, clinical and biobank research platforms with standardised variable measurements using a unique identification number per person.
* Detailed pedigree records facilitating research across multiple generations.
* Custom-designed framework for KWDSS, KEMReS and Keneba Biobank databases with: user-friendly interface for use by low-IT-skilled health professionals, lab and field staff; coded data rather than free text and lists facilitating ease of data management, clear patient/participant flow limiting missing data.
* Automated processes including the generation of consent and call lists; collection and logging of participant information on basic demographics, phenotypes and lab tests; collection, logging and tracking logging of biological samples.
* The majority of research platforms and ongoing studies now work on the basis of live/current direct data entry, thereby reducing the possibility of data errors.
* Large repository of banked biological samples.
* Established procedure for access to samples and data via KDSG and SCC/EC application.
* Good database and IT support.

**Weaknesses**

* The size of the total population of Kiang West (N~14000) is limiting for the study of e.g. rare diseases, diseases occurring infrequently in this population or sub-groups such as women who have never been pregnant, and there is a risk for ‘over studying’
* The KWDSS system also yields useful background data on the demographic status and changes in the area, although the population size is insufficient for some aspects of demographic research.
* The majority of longitudinal data is restricted to residents of the core villages (N~4000), with KW-wide (N~14000) data collections being more recent.
* There is some bias regarding the age-sex distribution between the ages of 20 – 50, due to (temporary) outmigration to urban areas for work (see Supplementary Figure 1). However, we increasingly conduct studies and follow-ups outside of the KW district.
* Whilst the mortality overall in the KW district is lower than the country average, the morbidity profile is comparable across The Gambia (see Tables 1 and 3)9.

**Can I get hold of the data? Where can I find out more?**

Access permission for collaborators is regulated via one or more of the following: PI(s) of platforms/research studies, Head of MRC Keneba Field Station or Head of MRC ING. Further details can be found via the MRC International Nutrition Group website. Access is controlled via the Keneba Database Steering Group (KDSG) and/or applications to joint Gambia Government/MRC Ethics Committee (SCC/EC).

**Figure legends** (figures submitted as separate files)

**Figure 1.** Map of the study area. The Kiang West (KW) district is located in the lower river division in The Gambia. Initial surveys were conducted in the core villages - Keneba, Manduar, Kantong Kunda and Jali (dark grey circles). The MRC Keneba field station now serves all villages in the district (light grey circles), captured by the KW Demographic Surveillance System (KWDSS). There are also two small government health centres (squares labelled M) in Kiang West. A midwife is stationed in Jiffarong and the nearest hospital is in Bwiam (square labelled H) outside the KW district on the main road to the coast (for more details see Supplementary Materials), respectively.

**Figure 2.** Schematic representation of time lines of data collection in Kiang West. Studies and surveys, especially those since 2000 are contained within the Kiang West Longitudinal Population Study (KWLPS) electronic databases.

**Figure 3.** Database structure and data flow for the Kiang West Longitudinal Population Study (KWLPS) cohort. For further details on the KWLPS databases see Supplementary Materials.

**List of Tables** (submitted as separate file)

**Table 1.** Summary statistics of the Kiang West Longitudinal Population Study (KWLPS) cohort in 2013 and The Gambia national data in comparison.

**Table 2.** Data collected in the Keneba Electronic Medical Records System (KEMReS) during each patient encounter.

**Table 3.**Ten most common clinical diagnoses made per age group between January 2010 and July 2014 at the MRC Keneba clinic.

**Table 4.** Data and samples collected as part of the Keneba Biobank.

**Supplementary materials** (submitted as separate file)

1. Abbreviations in main text and Supplementary materials
2. Supplementary Figures 1-3
3. Kiang West Longitudinal Population Study (KWLPS) Databases, additional information
4. Kiang West Demographic Surveillance System (KWDSSS) unique identification number
5. Keneba Electronic Medical Records System (KEMReS), additional information
6. Keneba Biobank, additional information
7. ‘Demography Search Using Bayes (DSUB) algorithm
8. References

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**Conflict of interest statement**

None declared.

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