

## REVIEW ARTICLE

# A review of the national response to CKDu in Sri Lanka

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**Abstract:** Since the mid-1990s, Sri Lanka's North Central Province has faced an increasing occurrence of renal disease. As the aetiology has not been elucidated, the disease is known as Chronic Kidney Disease of unknown aetiology (CKDu). This paper covers Sri Lanka's response to this debilitating and often fatal disease, and presents the chronology covering the national response. Further, the response has been covered from multiple angles, initially taking the broad national, political, private and international angle. Then a sectoral response analysis is presented, covering the medical, agriculture, food and nutrition, water, community and social sectors, as well as research and the media. Multiple action plans have been formulated and a consolidated action plan is currently being executed under HE the President. A brief response analysis is presented at the end. Many a hypothesis regarding the causative agents/risk factors for CKDu has been suggested by researchers. Research compilation on presented hypotheses for causing CKDu in Sri Lanka is also presented.

**Keywords:** Chronic Kidney Disease of Unknown aetiology, Sri Lanka.

## INTRODUCTION

At the turn of the new millennium, the North Central Province (NCP) of Sri Lanka had started recording a higher-than-normal number of patients with kidney disease (Ramachandran, 1994; Kudalugoda Arachchi *et al.*, 1999). In the year 2002, Anuradhapura district recorded the highest number of deaths from kidney failure in the island.

In 2000, a screening programme provided evidence on the emerging disease with the first cohort study (Athuraliya *et al.*, 2009). The affected individuals

are asymptomatic until late stages of the disease. Hypertension seems to be a late manifestation. The underlying histopathological feature is tubular atrophy and interstitial fibrosis without glomerular involvement until the late stages of the disease (Athuraliya *et al.*, 2011). In the absence of an identifiable causative factor, as in the case of conventional renal failure, such as hypertension, diabetes, snake-bite or leptospirosis, the term 'Chronic Kidney Disease of Unknown aetiology' (CKDu) was adopted. At present, records at the Epidemiology Unit identify around 20,000 CKDu patients with a population prevalence rate of 4.7% in the NCP alone. CKDu today is considered a major public health concern. A case definition for CKDu has been adopted by the Ministry of Health (Dassanayake & Herath, 2014), along with screening and clinical management guidelines for chronic kidney disease (CKD) and CKDu (MOH, 2014). World Health Organization (WHO) (2016) developed the surveillance scheme, which was not in place until 2016, in response to a need assessment.

The disease prevalence map has expanded (Figure 1) and presently it occurs in the North Central, North Western, Eastern and Uva Provinces of Sri Lanka. New foci have appeared and older ones have spread. Responses over a broader spectrum have emerged over time.

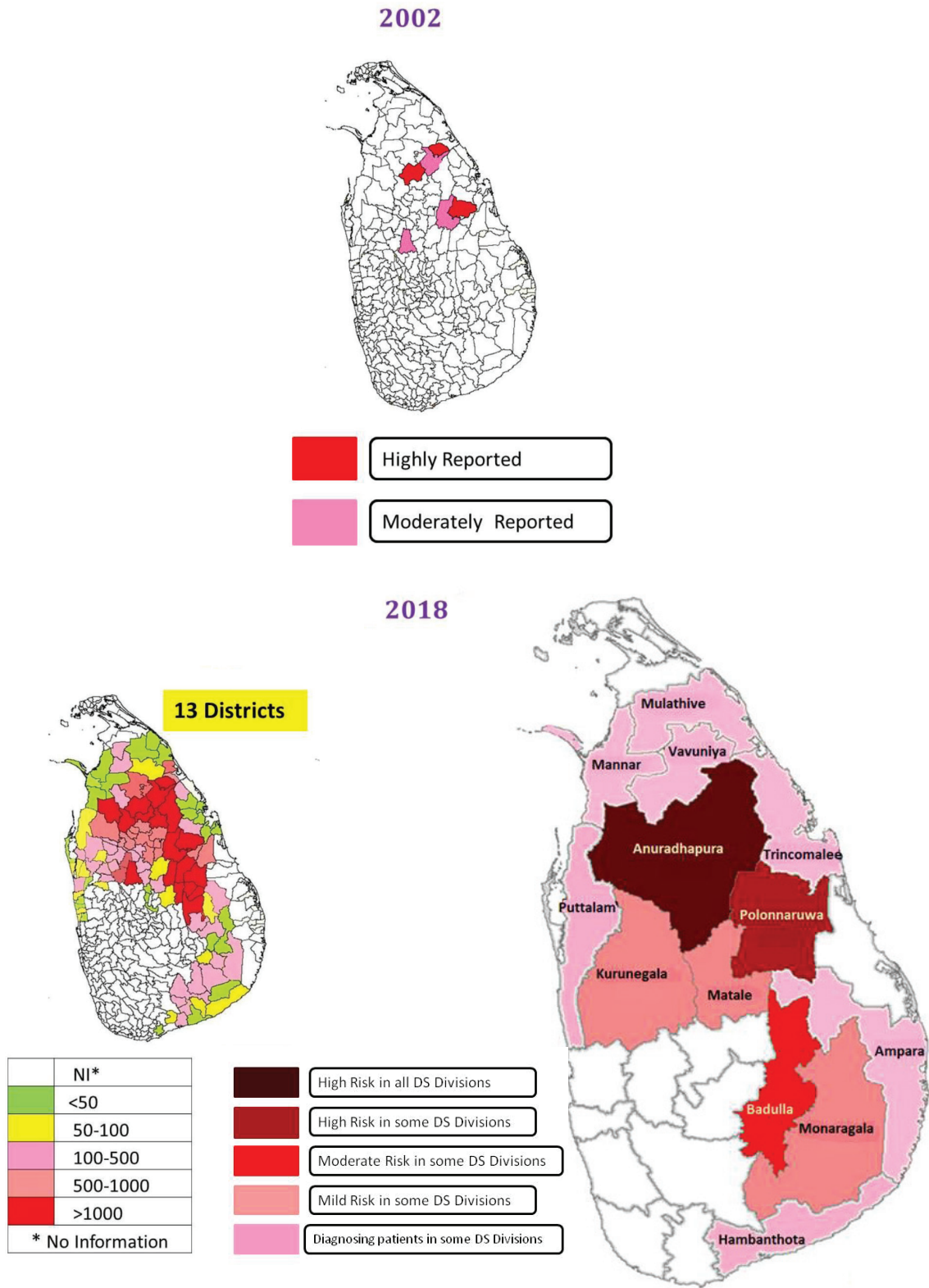
## NATIONAL RESPONSES

This section describes the broad response and the next section addresses the specific sectoral responses. Table 1 gives the national response in chronological order.

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**Figure 1:** Change in the prevalence of CKDu in Sri Lanka from 2002 to 2018  
 Source: Asanga Ranasinghe 2019, personal communication, 7 May.

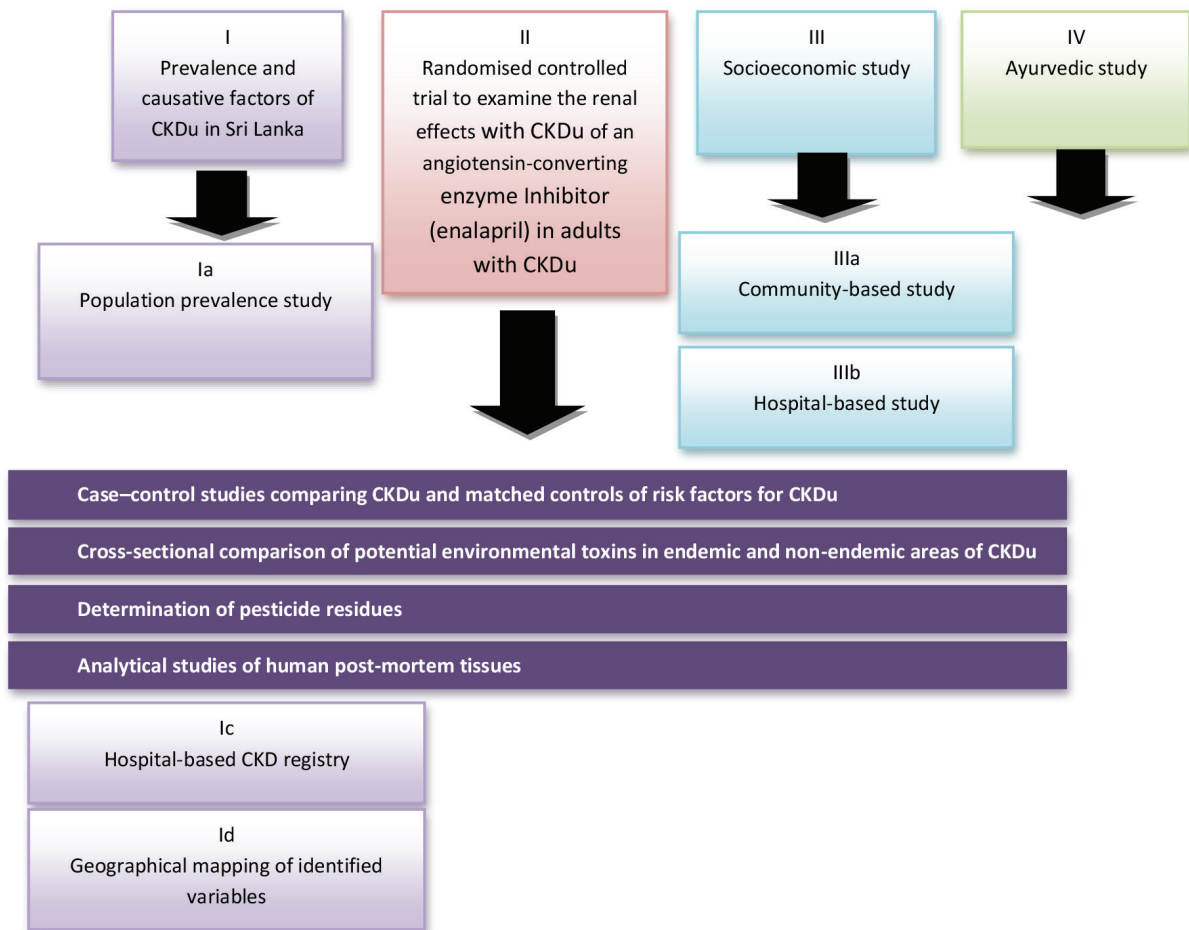
**Table 1:** Chronology of national response to CKDu

Year	Description
<b>1992</b>	Assistant Government Agent from Padaviya, NCP first informed Anuradhapura Hospital about his observation of an unusual number of deaths in his community
<b>2000</b>	First field report by a hydrogeologist on the water quality and specific kidney diseases in Morawewa–Gomarankadavela–Kepitigolewa areas (Lapègue, 2000)
<b>2002</b>	Establishment of the Renal Care and Research Centre at Medawachchiya
<b>2006</b>	First hypothesis on CKDu published in the <i>Ceylon Medical Journal</i> (Peiris-John, R. J. <i>et al.</i> , 2006)
<b>2007</b>	Minister of Health and Nutrition requests technical assistance from the World Health Organization (WHO), Geneva
<b>2008</b>	National Kidney Foundation of Sri Lanka (NGO) launched a programme to establish a Renal Care and Renal Research Centre at Anuradhapura General Hospital as a public-private venture
7 May	MOH and WHO Joint Seminar on Unusual Occurrences of Chronic Kidney Disease in Sri Lanka, Blood Bank Auditorium, Colombo
3–5 August	WHO consultation meeting on the research proposal to Government of Sri Lanka (GoSL), Giritale
September	Water Resources and Research Training Centre opened at Anuradhapura (built by Brandix and handed over to the Water Resources Board)
2 October	WHO partners' meeting organised by the WHO Country Office seeking donor assistance, Colombo
<b>2009</b>	
June	WHO/National Science Foundation (NSF) joint proposal submitted to the Department of National Planning WHO finalises and launches the national research programme
<b>2010</b>	
20 June	MOH and WHO joint workshop on implementing a National Cadaver Kidney Transplant Programme in Sri Lanka, Colombo
September	Renal Prevention and Renal Care Unit established at NCP
<b>2011</b>	
22 March	First water supply pilot project by the National Water Supply and Drainage Board (NWSDB) based on reverse osmosis (RO) started at Billewa, Anuradhapura district as a World Water Day event
<b>2012</b>	
11 March	Sri Lanka Medical Association (SLMA) Research Symposium on Chronic Kidney Disease of unknown aetiology (CKDu)
18 October	Inter-ministerial committee appointed to review indiscriminate use of chemical fertilizers and agrochemicals, inter-ministerial officials' committee appointed for CKDu (ministry secretaries), 4 subcommittees appointed by the ministerial/officials' committee
November	Parliamentary advisory committee set up on agriculture focusing on CKDu
23 December	First Presidential Task Force on CKDu established to drive the action plan prepared over a 5-year period with the Ministry of Special Projects (MSP) National Renal Registry established (Renal Registry Sri Lanka [website])

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<b>2014</b>	
22 December	Banned sale of glyphosate, carbofuran, propanil, carbaryl, chlorpyrifos in part of the country
<b>2015</b>	
04 February	Thirtieth hypothesis on CKDu published (Manthritilake, 2015) Cabinet submission on prevention of further spreading of CKD and providing welfare to the present kidney patients and their families, by the Minister of Social Services, Welfare and Livestock Development
11 February	Establishment of the second Presidential Task Force on CKDu in the Presidential Secretariat by cabinet decision
February	Fund-raiser event for the National Kidney Fund with HE the President in attendance
26 March	MOU signed between the Government of Sri Lanka (GoSL) and the Republic of China to construct a nephrology hospital in Polonnaruwa
22 May	Workshop on developing an action plan to prevent CKDu by the MSP, Colombo
28 May	Organization of Professional Associations (OPA) Think Tank Meeting — Strategies to arrest the occurrence and spread of CKDu, Hector Kobbekaduwa Research and Training Institute (HARTI), Colombo
15 June	Establishment of the Niroga lottery by the National Lotteries Board to raise money for the National Kidney Fund
24 June	Establishment of the National Kidney Fund CKDu Prevention Unit of NCP empowered island wide and brought under the MOH
29 July	Meeting with foreign dignitaries and organisations at the Presidential Secretariat to request support in eradicating CKDu in Sri Lanka, by HE the President
September	Opening of the first RO plant established by the second Presidential CKDu Task Force at Welioya
23 October	Islandwide ban on use of glyphosate
15 November	Suvodaya opening – a half-way home for kidney patients at Sarvodaya district centre, Anuradhapura
16 December	National workshop on CKDu roadmap organised by the CKDu Task Force in Colombo
<b>2016</b>	
	Through Budget proposals, NSF was assigned with supporting research related to four key areas of health importance, one being CKDu. Consequently, the Research Programme on Health Science (RPHS) was initiated by NSF.
15 Feb	Task Force convened meeting on National Plan for Chronic Kidney Disease Prevention (2016–2018), Colombo
08–10 March	World Kidney Day national function in Medawachchiya, Anuradhapura targeting school children on awareness and screening
March	GoSL launches the “A Toxin Free Nation” programme – related to the use of agrochemicals and agriculture production
26 April	WHO-supported Workshop to Media personnel on CKDu
27-29 April	International Expert Consultation on Chronic Kidney Disease of unknown aetiology
10 May	WHO-supported Workshop to Senior Media Personnel on CKDu
31 May	Handing over of Action Plan and the Way Forward to HE the President
24-25 October	WHO-supported panel on finalising case definition and surveillance program
<b>2017</b>	
July	WHO-supported workshop on an updated definition for CKDu
<b>2018</b>	
July 21	The start of the construction of China-Sri Lanka friendship hospital in Polonnaruwa. This specially targets treating kidney diseases and is expected to be the largest kidney hospital in South Asia
Sep 28	Launch of the construction of a state-of-the-art water testing laboratory at University of Peradeniya with the aim of finding a scientific solution to end CKDu. This is a joint Sri Lanka – China endeavour and will be the largest water testing laboratory in South Asia



**Figure 2:** WHO Research Programme on National Research Effort for CKDu – summary of WHO research components  
Source: World Health Organization (2013: p. 10).

## Government response

As the disease burden grew, the impact on the society also grew considerably. The initial response was to mobilise the state infrastructure. Specific task lists were coming in as recommendations from line ministries which were then consolidated into specific national responses. As the impact grew and the aetiology remained unknown despite studies, the Government requested the WHO for technical assistance. The intentions of the Government were twofold — to review the available data and initiate a coordinated, multisectoral research effort. The WHO acceded and the project was launched with majority of the financing (70%) coming through the approval of the cabinet via the National Science Foundation. Figure 2 illustrates the WHO study plan. With the submission of the WHO report (World Health Organization, 2013), the recommendations (Annex 1) were followed up again, with several line ministries playing a key role.

The Ministry of Special Projects (MSP) too was created, with CKDu as one of the two main areas of work, and was entrusted with coordinating the task with other ministries. Subsequently, the First Presidential Task Force on CKDu was created to work with the MSP on the suggested programmes. The State expenditure per year on CKD/CKDu was more than the budget provision for higher education, up to 2016 (Sri Lanka, Department of National Budget, 2016). The Government response resulted in four ministries in principle (Ministry of Health, Ministry of Agriculture, Ministry of Water Supply and Drainage, and Ministry of Social Services), developing and running programmes in support of four specific areas after consolidating the various schemes suggested. There had also been recommendations after review meetings from professional and scientific bodies in Sri Lanka, namely, the National Academy of Sciences – Sri Lanka (NASSL) and Organization of Professional Association (OPA, 2015).

The establishment of Presidential Task Forces highlighted the fact that the State understood the urgency as well as the importance of centralised coordination. The First Presidential Task Force was active for two years and the second is currently in force (Sri Lanka Presidential Task Force, 2016). The State has specifically allocated money, both for response and research, through the national budget, as it has identified CKDu as a national emergency. These funds are in addition to what has been received from donor agencies.

Setting up of the National Kidney Fund (de Silva, 2015) by the Government enables donations to be made by interested donors, organisations and well-wishers. The Fund also receives 10% of the proceedings from the National Lottery “Niroga”.

### **Political response**

As the disease prevalence was found to be higher in the poor socioeconomic segment and farming community, there was a direct response from politicians, irrespective of party affiliations. Observing the magnitude and growth of the problem, successive governments worked towards seeking for a solution as well as providing support to the affected communities. The mechanism for this was primarily through the line ministries and seeking overseas assistance by raising the issue at every opportunity. For those who were not in power, the pathway for action was to pressurise the Government to respond by highlighting issues at the ground level.

The political establishment acted speedily in imposing a ban on pesticides, especially, the herbicide, glyphosate. Sri Lanka became the second country in the world to enact a complete ban. The technical process followed by the Pesticide Technical Advisory Committee has not been published. There was no specific instance of the political system making use of professional opinion in a collective manner (Sri Lanka, National Academy of Sciences, Sri Lanka, 2013). Professionals from specific sectors were well-represented in the various committees setup by the Government and they had the opportunity to influence decision-makers in taking correct and scientific decisions. The President has appointed two popular Sri Lankan sportsmen as brand ambassadors to involve in fund raising activities to strengthen the Kidney Fund that is being operated by the Presidential Task Force.

### **Local government response**

In Sri Lanka’s constitution, health is a devolved subject; thus, the provincial government too has responsibility for health. Local governments have responded to

CKDu across endemic areas. There is widespread use of traditional medicine in these endemic areas. Both health systems have worked together, for instance, in carrying out awareness. With direct linkages to the affected communities, the local government had a larger share in the social response than the central government. Provincial health administration with its network of hospitals are much more closer to the disease hot spots.

The provincial health ministry at NCP has set up the Renal Prevention and Renal Care Unit with a medical officer, two research assistants and a health education officer. The Unit initiated the development of a database with the use of Geographical Information Systems (GIS) technology. Other provinces have not emulated this.

A large number of government extension workers support various sectors at the local level (from public health inspectors to enterprise development officers). However, in order to drive interventions at the ground level, effective coordination with suitable empowerment has been missing, as these individuals come under different line ministries. Indigenous medical practitioners have implemented various programmes related to the management of ill-health and health promotion with regard to CKDu at the grass-root level. Ayurvedic practitioners are sensitive to the proposal that the use of aristolochic acid may be a causal factor. The local government supports community-based organisations (CBOs) that work with people affected by CKDu at the village level.

### **Private sector response**

The private sector has supported some of the activities of the ministerial action plans. Principally, the private sector has engaged in the supply of filtration devices, having seen the role it can play in the provision of potable water. The private sector has been increasingly engaged in supply of Reverse Osmosis (RO) machines to home filtration systems. An example from the agriculture sector is the development of a biofilm biofertilizer production facility by a private company (Biofilm, 2016), based on research from the National Institute of Fundamental Studies. This is an innovative approach to improve soil fertility without resorting to chemical fertilizers. A percentage of the sales go to the National Kidney Fund. The Water Resources and Research Training Institute of the Water Resources Board at Anuradhapura was supported by a leading textile firm, as a corporate social responsibility (CSR) activity. This centre is engaged in ground water quality assessment of the NCP since 2010. Companies have also supported various medicare activities in endemic areas under the CSR function.

## International response

CKDu is not unique to Sri Lanka as there are a number of countries facing this issue. As the problem escalated, Sri Lanka reached out to the international community. Governments as well as international non-governmental organisations have extended support, starting with Poland, when the WHO brought in the donor community seeking support in Colombo. Recently, significant support has come from the Chinese Academy of Sciences and the Chinese Government. The latter has pledged to build a fully equipped hospital dedicated to renal diseases in Pollonnaruwa. The Chinese Academy of Sciences initiated a research programme with the University of Peradeniya, which has now been completed. A state-of-the-art water quality laboratory in the University of Peradeniya is about to be launched, supported by China. Researchers and analytical support have been received from various countries, such as Sweden, United States, India, Australia, New Zealand, Germany and Japan. Japanese support to the National Water Supply & Drainage Board (NWSDB) resulted in the publication of a groundwater quality atlas, which has a separate section on CKDu (Kawakami *et al.*, 2014).

Initially, Sri Lanka lacked some of the advanced analytical equipment required to carry out sample analysis. In the WHO study, some of the analytical investigations were conducted at the Antwerp University, Belgium. Samples collected during the WHO study were stored with the Medical Research Institute for future requirements. Local researchers have used Japanese facilities for the analysis of heavy metals, biopsy studies, etc. This situation has changed today with the availability of advanced instrumentation facilities at the Sri Lanka Nanotechnology Institute as well as with some universities (e.g. Peradeniya, Colombo).

The Water Supply Project, launched in 2016 for providing piped water to endemic areas by the Ministry of City Planning and Water Supply, is supported by Japanese aid. Participation of the diplomatic community can be witnessed at some of the State-supported events directed at CKDu. The Government considers this as an encouraging sign of a positive international response.

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## SECTORAL RESPONSES

### Health sector

The response of the health sector has been primarily three-fold; prevent, detect and manage. The seven strategies of the Ministry of Health regarding CKD/CKDu are as follows:

1. Access to screening
2. Management of patients
3. Improvement in human resources
4. Surveillance of CKD/CKDu patients
5. Community involvement
6. Intersectoral collaboration
7. Strengthening evidence-based management

In 2000, Sri Lanka had only two nephrologists in the health service; the number is expected to rise to 30 shortly. A nephrologist was first appointed to the NCP only in 2009. In 2015, the Epidemiological Unit of the Ministry of Health recommended the adoption of the urine protein sulfosalicylic acid precipitation test (SSA) or dipstick test for screening in a field setting, based on the operational feasibility which, however, differs from the method recommended by the Ministry of Health in 2014. Falling back on a less accurate mechanism may be due to lack of finances to support efficient screening. The distances that patients have to travel in the NCP, that also with much difficulty, are significant and this prevents people from responding to calls for screening. At present, there is only one screening vehicle but eight more are planned for 2020. Continuous Ambulatory Peritoneal Dialysis (CAPD) is available today for patients. The Government is also bringing in the scheme of cadaver transplants to meet the demand. Graft survival was found to be 93.2% at one year, 88.9% at 3 years and 84.6% at 5 years in a cohort study done on cadaveric renal transplants in the Kandy Hospital (Harrischandra *et al.*, 2017).

As time passed without the emergence of a clear medical answer, some patients have shifted back to indigenous medicine. There are also instances of communities seeking solutions through ritual practices.

### Water supply

Water has been linked to the disease by many a researcher. Liyanage & Jayathilake (2009) reported that there were disease-free pockets. The case of Gonamariyawa and Medawachchiya is an example. The conditions between Medawachchiya and Gonamariyawa vary in one aspect — the source of water to the community. The community at Gonamariyawa uses a spring well. Anuradhapura town is also free of CKDu. This area is served by piped water sourced from three tanks. Dissanayake *et al.* (2012) demonstrated that CKDu was geographically distributed in five areas of Sri Lanka. The affected villages were located below the level of reservoirs and canals, indicating the possibility of irrigated water draining to shallow wells, which serve as the main sources of drinking water. Gunatilake & Udeshani (2019) found

poor water quality, mainly in CKDu prevalence areas, in Monaragala district. Thus, at an early stage of the disease, the disease-water nexus was identified to direct much of the response.

Clinicians have noted the possibility of delaying the progression of the disease if the patient is supplied with clean drinking water. Methods such as rainwater-harvesting systems, reverse osmosis (RO) systems, and systems based on electrocoagulation have been implemented at the village-level for water supply. Individual household-level water filter units are also popular. Most communities in this region are familiar with household filter units, as work was earlier done on clay-based filters to support defluoridisation to counter the prevalence of dental and skeletal fluorosis, and fluoride is still considered a causative agent for CKDu as well. It is, however, known that the adoption of clay-based filters did not find widespread acceptance.

The Ministry of City Planning and Water Supply, together with the NWSDB and the National Community Water Trust, have short, medium and long-term plans to provide safe drinking water. The short-term strategy has been to provide CKDu-affected areas with good quality water for drinking and cooking purposes (a per capita supply of 5L per day). The accepted short-term processes are as follows:

1. Establishing small RO plants to purify groundwater from wells or bore holes and supply the community using bowzers. These units will be operated by community-based organisations (CBOs);
2. Providing bowser supply from existing water supply schemes;
3. Extending services whenever possible from existing piped water supply services;
4. Rainwater harvesting when bowser supply is uneconomical.

According to the NWSDB, following installation of the RO project at Billewa, the health status of patients has improved and some have even recovered subsequent to receiving quality water. However, no proper study to prove the fact was carried out. At present, there are 156 RO plants at the village-level, mostly operated through CBOs; 271 schools have also been equipped with RO systems. The NWSDB also has a well-screening programme. The Lanka Rainwater Harvesting Forum established the first scheme at Polpitiyagama (Kurunagala district) where 150 tanks were installed. At present, 2008 rainwater-harvesting systems are in

place (S. Sumanaweera 2018, personal communication, March).

No authoritative study is available on the technology option most suitable at ground level to provide quality water. Jayaweera *et al.* (2016) have considered nanofiltration. Rathnayake *et al.* (2016) have examined the use of domestic RO systems. The preferred choice at present is the RO technology, and the government has directly identified RO as the method of choice and allocated Rs. 900 million for it under the 2014 National Budget. Jayasinghe *et al.* (2015) carried out a monitoring study of RO system applications in CKDu-endemic areas and identified some shortcomings. The main recommendations were streamlining the installation mechanism, proper pre and post-locational evaluation and retentate management, and the broader health issues of drinking pure RO water (without a remineralisation stage). In many an instance what had been observed was direct discharge of retentate to the ground. Other recommendations were as follows:

1. Carry out investigative research urgently on the suspected health impacts of drinking RO water.
2. Develop a mechanism for supply of clean water on a large scale, especially for CKDu-affected areas as well as to other areas with water scarcity.
3. Revive the ancient tank system in the dry zone of the country in order to supply non-contaminated water, especially from agrochemicals.

In addition to RO systems, the NWSDB has provided 618 Grama Niladhari divisions with bowser water, where 4,090 bowser supply points are in operation (S. Sumanaweera 2018, personal communication, March). In addition, the pipeline of the existing water supply system has been extended by 518 km (S. Sumanaweera 2018, personal communication, March).

### **Agriculture sector**

Since the 1940s, fertilizers and pesticides have been used for agriculture in Sri Lanka. In 1962, subsidy schemes were introduced in agriculture. Sri Lanka is a significant user of both fertilizers and pesticides. There is a perception that since the subsidy of Rs. 350 per kg started in 2005, the quality of the incoming material has deteriorated, whereas the application rates have increased. Thus, when the “mystery disease” appeared, a direct linkage was made to the use of chemical fertilizers and pesticides. The concept of “poison-free foods” (meaning foods without hazardous chemicals in them) is appealing and a three-year national programme ‘A Toxin

Free Nation' has been launched by the GoSL. For quite a while, the use of compost for agriculture was promoted, and poor-quality compost had prevented the adoption of compost from municipal waste compost-sites being accepted in agriculture. As an answer to limiting the occurrence of CKDu, in 2014, the Ministry of Special Projects promoted the cultivation of traditional rice varieties over 50000 acres in the NCP. These varieties are resistant to pests and believed to also possess some medicinal value.

The Food and Agriculture Organization (FAO) has helped to establish a state-of-the-art laboratory in the Office of the Registrar of Pesticides, which should be able to support more active analytical interventions. In addition to glyphosate, three other pesticides that are known to be nephrotoxic have been banned.

### Food and nutrition sector

Attention was paid to the food consumption patterns of people in CKDu-endemic areas because of the knowledge of *itai-itai* disease in Japan and heavy metals in rice in Thailand. The emergence of hypothesis of cadmium in rice and in freshwater fish (i.e. Tilapia) in these areas caused quite an impact at the local level. The WHO (2013) highlighted selenium deficiency as a possible factor and cautioned against the consumption of lotus roots (*N. nucifera*). Farmers in the field drink from polluted streams and consume sugary tea, which also have been highlighted as possible causes, as some researchers believe extra sugar with limited water intake can be a causative factor (unpublished data). In affected families, lower nutritional levels have been identified.

The use of low-quality aluminium-based cookware and lead for soldering these were other issues that were identified. This has led to a switch to clay-based cooking utensils and government programmes, such as the distribution of clay pots to communities by the Ministry of Indigenous Medicine.

Production of indigenous rice varieties with known resistance to toxicity, which have additional health benefits, is a response by the food and nutrition sector, as stated in the previous section.

### Education sector

As the cause of CKDu is unknown, prevention had been identified as a possible course of action. However, it is difficult to state what constitutes prevention. As the awareness and knowledge of CKDu grew, there was a need for proactive communication and proper information on potential risk factors to the community. The Health

Education Bureau of the Ministry of Health has designed a communication strategy. At present, the local health departments conduct educational programmes through village health committees.

Considering that students are affected directly when a family member has CKDu, education with psychosocial support is necessary. No specific curricular measures or local school-level responses could be identified.

### Social sector

CKDu is prevalent largely in the age group of 30-60 years. With the breadwinner of the family affected, the whole family is impacted. There is consequently a significant social burden. Though Sri Lanka has an extended family system as well as support networks, the ability for such mechanisms to be effective diminishes in the case of CKDu, as the disease spreads across the whole village community. The WHO (2013) included the socioeconomic aspects in their larger study.

At the village level, CBOs provide a framework for assistance and support. One development is the establishment of Health Aid Societies. The Divisional Secretariat of the area provides financial assistance to these societies.

Transport services for patients to travel to healthcare centres are important. The provision of accommodation facilities for those who cannot afford frequent travel is also an important welfare measure. An example is Suvodaya from Sarvodaya in Anuradhapura. There was a rule that the grant of Rs. 3000 per month per patient from the Ministry of Social Services at the time be stopped once the patient died, but this rule is in effect since 2015. The amount of the grant was also increased to Rs. 5000 per month per patient from 01<sup>st</sup> June 2017 only in the endemic areas, and the arrangements are underway to provide it to all the patients in the island before the end of 2019 (A. Iddawela 2019, personal communication, January).

### Community response

Two types of community responses could be identified: the response coming from within the immediate community and that from afar. The latter is primarily philanthropic. The National Kidney Foundation is an option available for citizens in general and the Anuradhapura Renal Prevention and Renal Care Centre is an outcome of such activities.

The disease has had a significant social cost. In a family, it is usually the breadwinner who falls ill,

critically affecting the entire family. In a village, families are helped by their relatives and can depend on others' support. However, when multiple families in close proximity are affected, these networks of support are severely strained, considering the poor socioeconomic status that prevails. Mulleriyawa (2015a) has emphasised the need for a social worker with an understanding of the ground realities. Indigenous medical practitioners as well as religious organisations have contributed. Farmer communities have their own organisations and villages have rural development societies. The two main appeals from CBOs are usually for financial support and livelihood opportunities.

People have volunteered when certain community schemes have been established. Mulleriyawa (2015b) reports a pilot project setup within a high CKDu-prevalence area with the approval of the regional health authorities, where the community was provided with water from rainwater-harvesting and the cohort was to be monitored over a period of three years. The staff of the project comprises volunteers from the affected community. This project had three objectives:

1. Determine whether improving the quality of drinking water prevents/mitigates CKDu.
2. Ascertain whether rainwater-harvesting can provide adequate water for drinking and cooking purposes of a rural household throughout the year.
3. Develop viable strategies for making health education and agricultural extension more effective at the village level.

### Scientific and research response

The disease has been researched for over two decades. Sheriff & Janakan (2013) compiled an important literature repository covering CKDu for the period 1998–2013. The collection covered both peer-reviewed literature and literature from the open press. With the end of the WHO/National Science Foundation project, the work did not continue until the Coordinating Secretariat for Science Technology and Innovation (COSTI) enabled a digital repository for CKDu under its Basecamp as well as the Virtual Information Knowledge System (VIKS). While the Basecamp collection is available only to the user group (around 400 who have an active interest in engagement with CKDu), the VIKS is available to all (Sri Lanka, COSTI, VIKS, 2016). There is almost no voluntary participation in bringing information and findings to a central collection. The effort has to be made by those engaged in the task. The repository needs to be manned by implementers and planners.

Research is continuing in many places. When reviewing the published and unpublished literature on CKDu in Sri Lanka, it was observed that three community-based studies reported on the prevalence of CKDu in endemic and non-endemic areas (Athuraliya *et al.*, 2011; Wanigasuriya *et al.*, 2011; Jayatilake *et al.*, 2013). Jayasekara *et al.* (2012) did Geographical Information Systems (GIS) and Global Positioning Systems (GPS) mapping of 11630 patients in the affected areas. GIS mapping indicated five high prevalent areas in the region, namely, Medawachchiya, Padaviya, Girandurukotte, Medirigiriya and Nikawewa (Jayasekara *et al.*, 2012). The clinical studies suggested a higher probability of a tubular lesion (Athuraliya *et al.*, 2009; Athuraliya *et al.*, 2011) and tubulo-interstitial disease was the main finding on light microscopy of a biopsy study on 26 patients (Athuraliya *et al.*, 2011). Nanayakkara *et al.* (2012) also reported interstitial fibrosis and tubular atrophy as the histopathological features, based on 57 biopsies. Wijetunge *et al.* (2013) confirmed this finding as they observed that interstitial renal disease was 87% in a case series of 234 patients who underwent biopsy for confirmation of CKDu between 2004 and 2011 in Kandy and Anuradhapura hospitals. Two studies have detected urinary biomarkers, namely, alpha-1-microglobulin (AIM) (Nanayakkara *et al.*, 2012) and beta-2-microglobulin (Siriwardhana *et al.*, 2014), of early renal damage among CKDu patients, while N-acetyl-beta-D-glucosaminidase (NAG) was elevated only among patients with stage 5 CKD (Nanayakkara *et al.*, 2012).

The Sri Lanka Institute of Nanotechnology, with the support of the Ministry of Science, Technology and Research, is working on a home filtration unit with the ability to provide clean drinking water. The Nanyang Technological University of Singapore is providing membrane technology. Different universities are looking into this in different ways, according to the University Grants Commission which looked at how the research community can be mobilised to find a solution, following the WHO report. Government-allocated research money reaches the research community through the National Research Council and the National Science Foundation, both of which have dedicated fund lines available to support research in CKDu.

There has been criticism of research based on data from the community and from hospitals being perused separately, i.e. social studies and medical studies using two different datasets. For example, data pertaining to those who may be accessing indigenous medicine is usually not available. Interestingly, the WHO (2013) study reports that more women had the disease, although

**Table 2:** Research studies on possible risk factors for CKDu—the compilation of published hypotheses

Hypothesis	Publication	Primary institute* for this research
Drinking well water	Wanigasuriya <i>et al.</i> (2007) Chronic renal failure in North Central Province of Sri Lanka: an environmentally induced disease.	University of Sri Jayewardenepura
Drinking water in the field	Wanigasuriya <i>et al.</i> (2011) Chronic kidney disease of unknown aetiology in Sri Lanka: is cadmium a likely cause?	-do-
Drinking reservoir water	Jayasekera <i>et al.</i> (2012) Effect of concentrated water from reservoirs of high prevalence area for CKD of unknown origin in Sri Lanka on mice.	University of Peradeniya
Landscape hydrogeology	Manthrilake (2015) CKDu: are we shooting the right target?	International Water Management Institute (IWMI)
Existing of a synergic effect especially among Cd, F and hardness of water	Wasana <i>et al.</i> (2017) WHO water quality standards Vs Synergic effect(s) of fluoride, heavy metals and hardness in drinking water on kidney tissues.	University of Peradeniya
Snake-bite	Wanigasuriya <i>et al.</i> (2007) Chronic renal failure in North Central Province of Sri Lanka: an environmentally induced disease.	University of Sri Jayewardenepura
Fungal toxins	-do-	-do-
Bacterial toxins	-do-	-do-
Cyanobacterial toxins	Dissananyake <i>et al.</i> (2011) The short term effect of cyanobacterial toxin extracts on mice kidney.	University of Peradeniya
Use of ayurvedic medicines	Wanigasuriya <i>et al.</i> (2007) Chronic renal failure in North Central Province of Sri Lanka: an environmentally induced disease.	University of Sri Jayewardenepura
Being treated for hypertension	Wanigasuriya <i>et al.</i> (2011) Chronic kidney disease of unknown aetiology in Sri Lanka: is cadmium a likely cause?	-do-
Use of non-steroidal anti-inflammatory drugs (NSAIDs)	Elledge <i>et al.</i> (2014) Chronic kidney disease of unknown aetiology in Sri Lanka: quest for understanding and global implications.	RTI International, North Carolina
Genetic predisposition	Wanigasuriya <i>et al.</i> (2007) Chronic renal failure in North Central Province of Sri Lanka: an environmentally induced disease.	University of Sri Jayewardenepura
Smoking	Wanigasuriya <i>et al.</i> (2011) Chronic kidney disease of unknown aetiology in Sri Lanka: is cadmium a likely cause?	-do-
Exposure to sun, heat stress and dehydration	Dissananyake <i>et al.</i> (2012) Renal tubular functions of farmers of high prevalence area for CKDu.	University of Peradeniya
Low selenium or other micronutrients in the diet	Jayatilake <i>et al.</i> (2013) Chronic kidney disease of uncertain aetiology: prevalence and causative factors in a developing country.	Ministry of Health, Sri Lanka
Maternal malnutrition	Elledge <i>et al.</i> (2014) Chronic kidney disease of unknown aetiology in Sri Lanka: quest for understanding and global implications.	RTI International, North Carolina
Low calcium intake	-do-	-do-

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Chronic undernutrition	Elledge <i>et al.</i> (2014) Chronic kidney disease of unknown aetiology in Sri Lanka: quest for understanding and global implications.	RTI International, North Carolina
Low body mass index (BMI)	-do-	-do-
Oxidative stress	Sayanthooran <i>et al.</i> (2014) Oxidative stress markers in chronic kidney disease: gene expression analysis in a Sri Lankan population.	National Institute of Fundamental Studies (IFS), Kandy
Augmenting effect of dehydration and history of malaria	Siriwardhana <i>et al.</i> (2015) Dehydration and malaria augment the risk of developing chronic kidney disease in Sri Lanka.	Rajarata University of Sri Lanka
Exposure to Hanta viral infection	Gamage <i>et al.</i> (2017) Serological evidence of hantavirus infection in Girandurukotte, an area endemic for chronic kidney disease of unknown aetiology (CKDu) in Sri Lanka.	University of Peradeniya
Organophosphates - Pesticides and fertilizers	Peiris-John <i>et al.</i> (2006) Exposure to acetylcholinesterase-inhibiting pesticides and chronic renal failure.	University of Sri Jayewardenepura
Cadmium	Senevirathna (2008) Chronic renal failure among farm families in cascade irrigation systems in Sri Lanka associated with elevated dietary cadmium levels in rice and freshwater fish (Tilapia).	University of Peradeniya
Fluoride and aluminium	Illeperuma <i>et al.</i> (2009) Dissolution of aluminium from substandard utensils under high fluoride stress: a possible risk factor for chronic renal failures in the North-Central province.	-do-
Prolonged exposure of the kidney to many ionic species	Jayasekera <i>et al.</i> (2012) The effects from concentrated water on reservoirs of high prevalence areas on CKD of unknown origin in Sri Lanka.	-do-
Chemical nephrotoxicity aggravated by arsenic, heavy metals	Dahanayake <i>et al.</i> (2012) Presence of high levels of arsenic in internal organs of deceased patients with chronic kidney disease of unknown aetiology (CKDu): three case reports.	District General Hospital Monaragala, Sri Lanka
	Fonseka <i>et al.</i> (2012) Hardness and presence of arsenic in aquifers of selected CKDu prevalent and other areas in Sri Lanka.	University of Kelaniya
Chemical nephrotoxicity aggravated by chronic repeated dehydration. Responsible chemicals are arsenic, heavy metals, herbicides	Jayasumana <i>et al.</i> (2013) Possible link of chronic arsenic toxicity with chronic kidney disease of unknown aetiology in Sri Lanka.	Rajarata University of Sri Lanka
Arsenic and cadmium	Jayatilake <i>et al.</i> (2013) Chronic kidney disease of uncertain aetiology: prevalence and causative factors in a developing country.	Ministry of Health, Sri Lanka
Glyphosate, hard water and nephrotoxic metals	Jayasumana <i>et al.</i> (2014) Glyphosate, hard water and nephrotoxic metals: are they the culprits behind the epidemic of chronic kidney disease of unknown aetiology in Sri Lanka?	Rajarata University of Sri Lanka
Multifactorial origin	Wanigasuriya (2012) Aetiological factors of chronic kidney disease in the North Central Province of Sri Lanka: a review of evidence to-date	University of Sri Jayewardenepura

\* The Institute to which the Principal Author of each paper is affiliated to.

till then the perception was that mainly male farmers in the region were affected, and there are many studies that confirm the earlier observation (Jayasekara *et al.*, 2012; Jayasekara *et al.*, 2015; Wanigasuriya *et al.*, 2011; Wanigasuriya, 2011), while some other studies indicate that there is no significant difference between male: female ratio being 1.3:1 (Athuraliya *et al.*, 2006 as cited by Gunatilake *et al.*, 2014). Redmon *et al.* (2014) also have reviewed the Jayatilake *et al.* (2013) study focusing on the CKDu case definition, endemic and non-endemic geographic area selection, population sampling design, multimedia sample selection, chemical constituent selection, field documentation and laboratory analytical methodologies employed by the study.

The Centre for Education, Research and Training in Kidney diseases (CERTKid) of the University of Peradeniya has a multisectoral, multidisciplinary research programme, set up by funds received from the national budget of 2015. It is conducting research on ways to improve the efficiency of screening and on different biomarkers. There are more than 30 hypotheses and no definitive agreement on the causal factor/s as yet. Table 2 provides a list of important research publications that have led to these hypotheses along with the primary research institute.

Gunatilake *et al.* (2014) critically reviewed the current scientific evidence of Chronic Kidney Disease of unknown aetiology (CKDu) but giving more emphasis to the chronic exposure to heavy metals associated with agricultural activities. Therefore, an unbiased meta-analysis of the present scientific information is indicated.

### Media response

The nature of the disease and its high impact caused interest in and coverage by the media, which has given prominence to most of the hypotheses from the research programmes without any analysis. Some hypotheses, which have caused controversy, have received more media coverage. These may have caused more confusion than clarity (Gunawardene, 2012), as some sections of the affected community are not literate.

The media could have been responsive in a positive manner. As water was highlighted to be a prominent causal factor, there was the issue of people not drinking sufficient quantities due to fear of getting the disease. With another hypothesis of dehydration leading to CKDu, there was the need to handle communications more professionally. There is also a belief that the likelihood of death is higher with dialysis. The local media's lack of scientific competence is a factor.

## CONCLUSION

The response to CKDu from all sectors has been considerable. In most cases, impact of the responses has not been assessed, as in the case of water supply. While state-of-the-art renal facilities have been established, the area of social support has received much less attention. Communication need to be much more responsible and relevant. The WHO study did not come to a conclusion. A critical look at the response indicates a lack of focused drive in identifying the cause of the disease, which is the most salient issue. The vision of the current Presidential Task Force is preventing and eradicating 'CKD', instead of preventing and eradicating 'CKDu'. In reality, preventing and eradicating CKD, which is a global issue of Non-Communicable Disease is beyond the scope of a Presidential Task Force. This shows lack of focus. Almost all hypotheses have been examined in isolation and not much validation or parallel work have been done. The WHO project identified additional research areas (renal biopsy study, study on early markers, animal slaughter house study, cyanobacteria study and ochratoxin, p-aminohippuric acid [PAH], and aristolochic acid analysis in urine and water), including the planned phase II study (randomised clinical trial to examine the renal effects with enalapril in adults with CKDu) (Jayathilake *et al.*, 2013), which has now been completed and published (Selvarajah *et al.*, 2016). There is a need to have quantifiable goals and mobilise funds to ensure execution. The currently available National Kidney Fund should be used strategically and quickly by putting the plan into action.

Water supply is a basic human right. It is ironic that the very province, i.e. NCP, that introduced hydraulic technologies in the ancient period is facing an issue of potable water today, as CKDu is linked by many to water quality.

There is a need to have an open data policy. There has been criticism for not sharing data and information openly, although a large population group faces this problem. Jayasinghe (2014) comments on the CKD-CKDu confusion and the biased sampling, lack of uniform laboratory study procedures and statistical approaches. This statement is not repudiated as most research stands alone without replication and validation. A climate of data exchange and collaborative research between the medical and non-medical sectors appears to be wanting.

There have been several attempts to develop national action plans. A coherent strategy and focused action plan are important. The recommendations of all these action

plans are important and are perhaps valid for good health, in their own right, irrespective of CKDu.

A nation-wide surveillance system should be set up. Currently, the Ministry of Health has 34 sentinel sites around the country, which report to the Epidemiology Unit. Emerging technologies should be introduced to realize this goal. GIS application and data analytics need to be markedly strengthened. CKDu provides an opportunity to understand and execute better response mechanisms, and the national response needs to be aware of the potential of positive and innovative responses.

Considering the time that has passed since the disease was first diagnosed in mid-1990s, the enormity of the burden and the continuously accumulating death toll, there is a definite need for the Sri Lankan national response to be informed by proper assessment of latest research on the subject.

## REFERENCES

Athuraliya, N. T. C., Abeysekera, T. D. J., Amerasinghe, P. H., Kumarasiri, R., Bandara, P., Karunaratne, U., Milton, A. H. and Jones, A. L. (2011) Uncertain etiologies of proteinuric-chronic kidney disease in rural Sri Lanka, *Kidney International*, 80(11), pp:1212-1221.

DOI: <https://doi.org/10.1038/ki.2011.258>

Athuraliya, T. N. C., Abeysekera, D. T. D. J., Amerasinghe, P. H., Kumarasiri, P. V. R. & Dissanayake, V. (2009) Prevalence of chronic kidney disease in two tertiary care hospitals: high proportion of cases with uncertain aetiology, *Ceylon Medical Journal*, 54(1), pp: 23-25.

DOI: <https://doi.org/10.4038/cmj.v54i1.471>

Biofilm (2014) [Online] Available from: <http://biofilm.lk/> [Accessed on 30<sup>th</sup> March 2016].

Dahanayake, K. S., Wijewardhana, K. M. .R. C., Jayasumana, M. A. C. S. and Paranagama, P. (2012) Presence of high levels of arsenic in internal organs of deceased patients with chronic kidney disease of unknown aetiology (CKDu): three case reports, In: Sri Lanka Medical Association, *Research Symposium on Chronic Kidney Disease of Unknown Aetiology (CKDu)*, Colombo, Sri Lanka, 11 March 2012, Colombo: Sri Lanka Medical Association [Online] Available from: [https://issuu.com/slmanews/docs/ckdu\\_abstract\\_book](https://issuu.com/slmanews/docs/ckdu_abstract_book) [Accessed: 8<sup>th</sup> December 2012].

DOI: <https://doi.org/10.4038/sljas.v24i1.7562>

Dassanayake, R. and Herath, N. (2014) *Clinical management guidelines CKD and CKDu*, Colombo: Ministry of Health.

de Silva, A. (2015) CKDu in Sri Lanka– has the management of the disease improved?, *The Island* [Online] 14<sup>th</sup> December,

Available from: [http://www.island.lk/index.php?page\\_cat=article-details&page=article-details&code\\_title=137016](http://www.island.lk/index.php?page_cat=article-details&page=article-details&code_title=137016) [Accessed: 11<sup>th</sup> April 2016].

Dissanayake, D. M., Jayasekera, J. M. K. B., Wimalasiri, R., Ratnayake, I. and Dissanayake, S. (2012) Renal tubular functions of farmers of high prevalence area for CKDu, In: Sri Lanka Medical Association, *Research Symposium on Chronic Kidney Disease of Unknown Aetiology (CKDu)*, Colombo, Sri Lanka 11 March 2012, Colombo: Sri Lanka Medical Association [Online] Available from: [https://issuu.com/slmanews/docs/ckdu\\_abstract\\_book](https://issuu.com/slmanews/docs/ckdu_abstract_book) [Accessed: 8<sup>th</sup> December 2012].

DOI: <https://doi.org/10.4038/sljas.v24i1.7562>

Dissananyake, D. M., Jayasekera, J. M. K. B., Ratnayake, P., Wickramasinghe, W. and Radella, Y. A. (2011) The Short-term Effect of Cyanobacterial Toxin Extracts on Mice Kidney, *Proceedings of the Peradeniya University Research Sessions*, 16.

Dissanayake, D. M., Jayasekera, J. K. M. B. Adhikari, S. B. and Bandara, P. (2012) Geographical distribution of Chronic Kidney Disease of unknown origin in Sri Lanka – is it related to stagnant irrigated water?, In: Sri Lanka Medical Association, *Research Symposium on Chronic Kidney Disease of Unknown Aetiology (CKDu)*, Colombo, Sri Lanka, 11 March 2012, Colombo: Sri Lanka Medical Association [Online] Available from: [https://issuu.com/slmanews/docs/ckdu\\_abstract\\_book](https://issuu.com/slmanews/docs/ckdu_abstract_book) [Accessed: 8<sup>th</sup> December 2012].

DOI: <https://doi.org/10.4038/sljas.v24i1.7562>

Elledge, M. F., Redmon, J. H., Levine, K. E., Wickremasinghe, R. J., Wanigasariya, K. P. and Peiris-John, R. J. (2014) Chronic kidney disease of unknown etiology in Sri Lanka: quest for understanding and global implications, *RTI Research Brief*, Research Triangle Park, NC, USA: RTI.

DOI: <https://doi.org/10.3768/rtipress.2014.rb.0007.1405>

Fonseka, S. I., Jayalath, K., Amarasinghe, M., Mahamithawa, A. M. P., Senanayake, V. K. and Paranagama, P. A. (2012) Hardness and presence of arsenic in aquifers of selected CKDu prevalent and other areas in Sri Lanka, In: Sri Lanka Medical Association, *Research Symposium on Chronic Kidney Disease of Unknown Aetiology (CKDu)*, Colombo, Sri Lanka, 11 March 2012, Colombo: Sri Lanka Medical Association [Online] Available from: [https://issuu.com/slmanews/docs/ckdu\\_abstract\\_book](https://issuu.com/slmanews/docs/ckdu_abstract_book) [Accessed: 8<sup>th</sup> December 2012].

DOI: <https://doi.org/10.4038/sljas.v24i1.7562>

Gamage, C. D., Yoshimatsu, K., Sarathkumara, Y. D., Kulendiran, T., Nanayakkara, N. and Arikawa, J. (2017) Serological evidence of hantavirus infection in Girandurukotte, an area endemic for chronic kidney disease of unknown aetiology (CKDu) in Sri Lanka, *International Journal of Infectious Diseases*, 57, pp: 77-78 [Online] Available from: <https://www.ncbi.nlm.nih.gov/pubmed/28212862> [Accessed: 12<sup>th</sup> December 2017].

DOI: <https://doi.org/10.1016/j.ijid.2017.02.004>

- Gunatilake, S. K. and Udeshani, W. A. C. (2019) Suitability of groundwater for drinking purposes using water quality indices in CKDu prevalence areas in Sri Lanka, Book of Abstracts-2<sup>nd</sup> International Conference on Future of Women '19 (Future Women 2019), pp: 26.
- Gunatilake S. K., Samaratunga, S. S. and Rubasinghe, R. T. (2014) Chronic Kidney Disease (CKD) in Sri Lanka- Current Research Evidence Justification: A Review, *Sabaragamuwa University Journal*, 13(2), pp: 31-58.  
DOI: <https://doi.org/10.4038/suslj.v13i2.7680>
- Gunawardene, N. (2012) *Mass kidney failure and mass media failure: insights from Sri Lanka* [Online] Available from: <https://www.slideshare.net/NalakaG/nalaka-gunawardene-mass-kidney-failure-mass-media-failure-17-oct-2012-14794600> [Accessed: 30<sup>th</sup> March 2016].
- Harrischandra, P. K., Jayatunge, D. N., Rambukwella, U. B., Sumithraarachchi, I. B., Karunadasa, U. I. and Abeyagunawardena, A. S. (2017) First experience of cadaveric renal transplantation in Sri Lanka, *Ceylon Medical Journal*, 62(2), pp: 83-86.  
DOI: <https://doi.org/10.4038/cmj.v62i2.8471>
- Hettiarachchi, K. (2014) Tackling kidney disease in NCP, *The Sunday Times* [Online] 27<sup>th</sup> April, Available from: <http://www.sundaytimes.lk/140427/news/tackling-kidney-disease-in-ncp-93909.html> [Accessed: 30<sup>th</sup> March 2016].
- Illeperuma, O. A., Dharmagunawardhane, H. A. and Herath, K. R. P. (2009) Dissolution of aluminium from substandard utensils under high fluoride stress: a possible risk factor for chronic renal failures in the North Central province, *Journal of the National Science Foundation of Sri Lanka*, 37(3), pp: 219-222.  
DOI: <https://doi.org/10.4038/jnsfr.v37i3.1217>
- Jayasekera, K. B., Dissanayake, D. M., Sivakanesan, R., Ranasinghe, A., Karunaratna, R. H. and Kumara, G. W. G. P. (2015) Epidemiology of chronic kidney disease, with special emphasis on chronic kidney disease of uncertain aetiology in the north central region of Sri Lanka, *Journal of Epidemiology*, 25(4), pp: 275-280.  
DOI: <https://doi.org/10.2188/jea.je20140074>
- Jayasekera, J. M. K. B., Dissananyake, D. M., Adhikari, S. B. and Bandara, P. (2012) Geographical distribution of Chronic Kidney Disease of unknown origin in Sri Lanka – is it related to stagnant irrigated water?, In: Post Graduate Institute of Science, University of Peradeniya, *International Symposium on Water Quality and Human Health: Challenges Ahead*, Peradeniya, Sri Lanka, 22-23 March 2012, Peradeniya: Post Graduate Institute of Science, p. 56 [Online] Available from: [http://www.pgis.pdn.ac.lk/watersym/docs/proceedings\\_2012.pdf](http://www.pgis.pdn.ac.lk/watersym/docs/proceedings_2012.pdf) [Accessed: 8<sup>th</sup> December 2012].  
DOI: <https://doi.org/10.17501/foodqualss.2017.1104>
- Jayasekera, J. M. K. B., Dissananyake, D.M., Ratnayake, P., Wickramasinghe, W., Radella, Y. A. and Palugaswewa, W. B. (2012) Effect of concentrated water from reservoirs of high prevalence area for CKD of unknown origin in Sri Lanka on mice, In: Sri Lanka Medical Association, *Research Symposium on Chronic Kidney Disease of Unknown Aetiology (CKDu)*, Colombo, Sri Lanka, 11 March 2012, Colombo: Sri Lanka Medical Association [Online] Available from: [https://issuu.com/slmanews/docs/ckdu\\_abstract\\_book](https://issuu.com/slmanews/docs/ckdu_abstract_book) [Accessed: 8<sup>th</sup> December 2012].  
DOI: <https://doi.org/10.4038/sljas.v24i1.7562>
- Jayasinghe, P., Herath, B. and Wikramasinghe, N. (2015) Technical review report based on a visit to Anuradhapura CKDu affected areas, In: COSTI: connecting Innovation [Online] Available from: <http://www.costi.gov.lk/index.php/en/2011-03-31-04-24-11?download=245:visit-to-anuradhapura-ckduaaffected-areas> [Accessed: 30<sup>th</sup> March 2016].
- Jayasinghe, S. (2014) Chronic kidney disease in rural areas of Sri Lanka: an evolving catastrophe needing an urgent response, *Ceylon Medical Journal*, 59(3), pp: 94-96.  
DOI: <https://doi.org/10.4038/cmj.v59i3.7470>
- Jayasumana, C., Gunatilake, S. and Senanayake, P. (2014) Glyphosate, Hard Water and Nephrotoxic Metals: Are They the Culprits Behind the Epidemic of Chronic Kidney Disease of Unknown Aetiology in Sri Lanka?, *International Journal of Environmental Research and Public Health*, 11(2), pp: 2125-2147.  
DOI: <https://doi.org/10.3390/ijerph110202125>
- Jayasumana, M. A. C. S., Paranagama, P. A., Amarasinghe, M. D., Wijewardane, K. M. R. C., Dahanayake, K. S., Fonseka, S. I., Rajakaruna, K. D. L. M. P., Mahamithawa, A. M. P., Samarasinghe, U. D. and Senanayake, V. K. (2013) Possible link of Chronic arsenic toxicity with Chronic Kidney Disease of unknown aetiology, *Sri Lanka Journal of Natural Sciences Research*, 3(1) [Online] Available from: <https://www.iiste.org/Journals/index.php/JNSR/article/view/4193> [Accessed: 30<sup>th</sup> March 2016].  
DOI: <https://doi.org/10.4038/mljssl.v3i1.7316>
- Jayatilake, N., Mendis, S., Maheepala, P. and Mehta F. R. (2013) Chronic kidney disease of uncertain aetiology: prevalence and causative factors in a developing country, *BMC Nephrology*, 14, 180.  
DOI: <https://doi.org/10.1186/1471-2369-14-180>
- Jayaweera, M., Rathnayake, N., Manathunga, J., Gunawardane, B. and Gunarathne, S. (2016) Removal potential of Cd, F, Al and excessive hardness in dietary intake (water in chronic kidney disease of unknown aetiology prevalent areas by household nanofiltration), In: Environmental & Water Resources Institute of the American Society of Civil Engineers (ASCE-EWRI), *8<sup>th</sup> International Perspectives on Water Resources and the*

*Environment Conference*, Colombo, Sri Lanka, 4-6 January 2016.

DOI: <https://doi.org/10.15242/ijaaec.er0116026>

Johnson, S. (2006) *The ghost map*, London: Penguin Books.

Kawakami, T., Motoyama, A., Nagasawa, S., Weragoda, S. and Chaminda, T. (2014) *Groundwater quality atlas of Sri Lanka*, Peradeniya: Sanduni Offset Printers.

Kudalugoda Arachchi, J., Lanerolle, R. D., Kathiriarachchi, A. K., Nanayakkara, S., Sheriffdeen, A. H. and Sheriff, M. H. R. (1999) Demographic characteristics of end stage renal diseases in Sri Lanka, In: Sri Lanka Medical Association, *112<sup>th</sup> Academic Sessions*, 1999, Colombo: Sri Lanka Medical Association.

DOI: <https://doi.org/10.4038/sljbm.v1i1.1478>

Lapègue, J. (2000) Field report on water quality and specific kidney diseases in Morawewa-Gomarankadavela-Kepitigolewa areas, *Action Contre la Faim Technical Report*.

Manthrilake, H. (2015) CKDu: are we shooting the right target? In: Water Resources Board (WRB) and Dam Safety and Water Resources Planning Project (DSWRPP), *Workshop on Importance of Groundwater Monitoring in Sri Lanka*, Colombo, 17 July 2015.

Mulleriyawa, R. (2015a) Living among CKDu patients, *Daily News* [Online], 06<sup>th</sup> January, Available from: <http://www.dailynews.lk/2016/01/06/features/living-among-ckdu-patients> [Accessed: 12<sup>th</sup> December 2017].

Mulleriyawa, R. (2015b) Pilot project on preventing chronic kidney disease, *The Island*, 16<sup>th</sup> December.

Nanayakkara, S., Komiya, T., Ratnatunga, N., Senevirathna, S. T. M. L. D., Harada, K. H., Hitomi, T., Gobe, G., Muso, E., Abeysekera, T. and Koizumi, A. (2012) Tubulointerstitial damage as the major pathological lesion in endemic chronic kidney disease among farmers in North Central Province of Sri Lanka, *Environmental Health and Preventive Medicine*, 17(3), pp:213-221.

DOI: <https://doi.org/10.1007/s12199-011-0243-9>

Nanayakkara, S., Senevirathna, S. T. M. L. D., Karunaratne, U., Chandrajith, R., Harada, K. H., Hitomi, T., Watanabe, T., Abeysekera, T., Aturaliya, T. N. and Koizumi, A. (2012) Evidence of tubular damage in the very early stage of chronic kidney disease of uncertain etiology in the North Central Province of Sri Lanka: a cross-sectional study, *Environmental Health and Preventive Medicine*, 17(2), pp: 109-117.

DOI: <https://doi.org/10.1007/s12199-011-0224-z>

OPA News (2016) OPA Launches two Books on “Chronic Kidney Disease Of Unknown Etiology (CKDu)” & “Role of Agriculture in Food Sovereignty and Poverty Eradication”, *OPA News* [Online] 14(01) February, p. 3, Available from: <http://opasrilanka.org/wp-content/uploads/2017/09/2016-February-newsletter.pdf> [Accessed: 12<sup>th</sup> December 2017].

Peiris-John, R. J., Wanigasuriya, J. K. P., Wickremasinghe, A. R., Dissanayake, W. P. and Hittarage, A. (2006) Exposure to acetylcholinesterase-inhibiting pesticides and chronic renal failure, *Ceylon Medical Journal*, 51(1), pp: 42-43.

DOI: <https://doi.org/10.4038/cmj.v51i1.1382>

Ramachandran, S. (1994) Renal diseases: Sri Lankan and global spectrum, *Journal of the Ceylon College of Physicians*, 27, pp: 27-35.

Ratnayake, N., Gunawardane, B., Manathunga, J., Jayaweera, M. and Sudasinghe, M. (2016) Is commercially available RO filtration capable enough to protect the health of subjects of chronic kidney disease of unknown aetiology?, In: Environmental & Water Resources Institute of the American Society of Civil Engineers (ASCE-EWRI), *8<sup>th</sup> International Perspectives on Water Resources and the Environment Conference*, Colombo, Sri Lanka, 4-6 January 2016.

Redmon, J. H., Elledge, M. F., Womack, D. S., Wickremasinghe, R., Wanigasuriya, K. P., Peiris-John, R. J., Lunyera, J., Smith, K., Raymer, J. H. and Levine, K. E. (2014) Additional perspectives on chronic kidney disease of unknown aetiology (CKDu) in Sri Lanka—lessons learned from the WHO CKDu population prevalence study, *BMC nephrology*, 15(1), 125.

DOI: <https://doi.org/10.1186/1471-2369-15-125>

Sayanthooran, S., Magana-Arachchi, D. N., Sooriyapathirana, S. D. S. S., Abeysekera, T. and Gunarathne, L. (2014) Oxidative stress markers in chronic kidney disease: gene expression analysis in a Sri Lankan population, In: Institute of Fundamental Studies, *2<sup>nd</sup> International Symposium on Driving Research Towards Economy: Opportunities and Challenges*, Peradeniya, 13–14<sup>th</sup> November, Kandy: Institute of Fundamental Studies.

DOI: <https://doi.org/10.17501/biotech.2016.1102>

Selvarajah, M., Mendis, S., Jayasinghe, S., Sheriff, R., Abeysekera, T. and Mehta, F. (2016) Randomized controlled trial of treatment of chronic kidney disease of uncertain aetiology with Enalapril, *Journal of Clinical Toxicology*, 6(1), 281.

DOI: <https://doi.org/10.4172/2161-0495.1000281>

Senevirathna, D. M., Dasanayake, D. M., Herath, V., Bandara, J. M., Abeysekera, T. and Rajapaksha, K. H. (2008) Chronic renal failure among farm families in cascade irrigation systems in Sri Lanka associated with elevated dietary cadmium levels in rice and freshwater fish (Tilapia), *Environmental Geochemistry and Health*, 30(5), pp: 465-478.

DOI: <https://doi.org/10.1007/s10653-007-9129-6>

Sheriff, R. and Janakan, N. (2013) *Literature repository on chronic kidney disease of unknown aetiology— CKDu 1998–2013*.

Siriwardhana, E. A., Perera, P. A., Sivakanesan, R., Abeysekera, T., Nuggegod, D. B. and Weerakoon, K. G. (2014) Is the staple

diet eaten in Medawachchiya, Sri Lanka, a predisposing factor in the development of chronic kidney disease of unknown aetiology? A comparison based on urinary beta2-microglobulin measurements, *BMC Nephrology*, 15(1), 103.

DOI: <https://doi.org/10.1186/1471-2369-15-103>

Sri Lanka, COSTI, Virtual Information Knowledge System (2016) [Online] Available from: <http://dSPACE.COSTI.gov.lk:8080/xmlui/handle/123456789/79> [Accessed: 30<sup>th</sup> March 2016].

Sri Lanka, Department of National Budget (2016) [Online] available from: <http://www.treasury.gov.lk/budget-estimates/budget-estimates-2016-approved.html> [Accessed: 30<sup>th</sup> March 2016].

Sri Lanka, Lanka Rain Water Harvesting Forum (2016) [Online] Available from: <http://lankarainwater.org/wp/> [Accessed: 30<sup>th</sup> March 2016].

Sri Lanka, Ministry of Health (2014) *Screening guidelines—chronic kidney disease Sri Lanka*, Colombo: Epidemiology Unit, Ministry of Health.

Sri Lanka, National Academy of Sciences (2015) NASSL Statement on the Banning of Glyphosate [Online] Available from: <https://nassl.org/nassl-statement-on-the-banning-of-glyphosate/> [Accessed: 30<sup>th</sup> March 2017].

Sri Lanka, National Academy of Sciences (2013) *Proceedings of the Symposium on Chronic Kidney Disease of uncertain aetiology (CKDu) – a scientific basis for future action*, 10 December 2013, Colombo: National Academy of Sciences.

Sri Lanka, Organization of Professional Association of Sri Lanka (2015) *OPA think tank recommendations to arrest the occurrence and spread of chronic kidney disease of unknown aetiology (CKDu)*.

Sri Lanka, Presidential Task Force (2016) *Chronic Kidney Disease Prevention* [Online] Available from: <http://www.presidentialtaskforce.gov.lk/en/kidney.html#> [Accessed: 30<sup>th</sup> March 2016].

Sri Lanka, Renal Registry Sri Lanka (2016) [Online] Available from: <http://renal.nicslk.com/> [Accessed: 30<sup>th</sup> March 2016].

Wanigasuriya, K. P., Peiris-John, R. J. and Wickremasinghe, R. (2011) Chronic kidney disease of unknown aetiology in Sri Lanka: is cadmium a likely cause?, *BMC Nephrology*, 12(1), pp: 32-38.

DOI: <https://doi.org/10.1186/1471-2369-12-32>

Wanigasuriya, K. P., Peiris-John, R. J., Wickremasinghe, R. and Hittarage, A. (2007) Chronic renal failure in North Central Province of Sri Lanka: an environmentally induced disease, *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 101(10), pp: 1013-1017.

DOI: <https://doi.org/10.1016/j.trstmh.2007.05.006>

Wanigasuriya, K. P. (2011) Update on Uncertain Aetiology of Chronic Kidney Disease in Sri Lanka's North-Central Dry Zone, *MEDICC Review*, 16(02), pp: 61-65.

Wanigasuriya, K. (2012) Aetiological factors of Chronic Kidney Disease in the North Central Province of Sri Lanka: A review of evidence to-date, *Journal of the College of Community Physicians of Sri Lanka*, 17(1), pp: 21-42.

DOI: <https://doi.org/10.4038/jccpsl.v17i1.4931>

Wasana, H. M. S., Perera, G. D. R. K., Gunawardena, P. de S., Fernando, P. S. and Bandara, J. (2017) WHO water quality standards vs Synergic effect(s) of fluoride, heavy metals and hardness in drinking water on kidney tissues, *Scientific Reports*, 7, 42516.

DOI: <https://doi.org/10.1038/srep42516>

Wijetunge, S., Ratnatunga, N. V., Abeysekera, D. T., Wazil, A. W., Selvarajah, M. and Ratnatunga, C. N. (2013) Retrospective analysis of renal histology in asymptomatic patients with probable chronic kidney disease of unknown aetiology in Sri Lanka, *Ceylon Medical Journal*, 58(4), pp:142-147.

DOI; <https://doi.org/10.4038/cmj.v58i4.6304>

World Health Organization (2016) *Workshop report on 'Designing a step-wise approach to estimate the burden and to understand the aetiology of CKDu in Sri Lanka'*.

World Health Organization (2013) *Investigation and evaluation of chronic kidney disease of uncertain aetiology*, Final report of Grant No. 57445 [Online] Available from: <http://www.indiaenvironmentportal.org.in/files/file/Chronic%20Kidney%20Disease%20of%20Sri%20Lanka.pdf> [Accessed: 30<sup>th</sup> March 2016].

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**Annex 1: The GoSL/WHO study recommendations (Recommendations to address CKDu based on the WHO final study report)**


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1. Since the determinants of CKDu lie outside the health sector, it is recommended to set up a high-level interministerial committee, to actively engage Ministries of Agriculture, Water Supply, Irrigation and Social Services to implement multisectoral policy action required to address the problem of CKDu.
  2. Despite the water being safe for use, water purification schemes need to be scaled up to provide adequate water to households in the endemic area for drinking and cooking purposes as it is a human rights issue.
  3. Strengthen the regulatory framework to improve quality control of imported agrochemicals, particularly with regard to those containing nephrotoxic agents such as Cd and As, amendments to existing legislation, capacity strengthening for implementation and monitoring.
  4. Implement and monitor comprehensive public health measures to reduce the exposure of farmers to harmful health effects of agrochemicals through,
    - i) education on the appropriate use of fertilizer
    - ii) compulsory provision of safety clothing, gloves and masks at the point of sale of agrochemicals
    - iii) control of the sale of agrochemicals which are known to be nephrotoxic e.g. Propanil, Chlopyrifos and others
    - iv) education on cooking practices i.e., avoid the use of water from irrigation canals for cooking and drinking, discard water after boiling rice, reduce intake of lotus particularly in families with a history of kidney disease
    - v) education on the importance of adequate water intake and non-smoking.
  5. Improve service provision for early detection of CKDu, hypertension and diabetes and appropriate treatment (avoiding nephrotoxic medications) including through close to client services.
  6. Increase the financial assistance provided to farmer families affected by CKDu to prevent them from getting more impoverished and malnourished. Inability to purchase food will cause iron, folate, antioxidant and trace metal deficiency which increase susceptibility to harmful effects of heavy metals on the kidney.
  7. Increase awareness among Ayurvedic practitioners of the nephrotoxic effects of *Aristolochia* (sapsanda) and recommend not using it.
  8. In the long term, regulate as necessary and facilitate research to; promote the use of alternative fertilizers, reduce heavy metals in soil or make them less available, develop rice strains which require less fertilizer / resistant to pests, reduce pollution of the environment including air pollution.
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Source: World Health Organization (2013; pp: 315-316).