Selected Health Consequences of the Chernobyl Disaster:

A Systematic Update of the Literature

2014 Report

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INTRODUCTION

The Chernobyl Nuclear Power Plant disaster began on April 26, 1986 when reactor 4 failed during a scheduled systems test. The catastrophe contaminated an area with radiation that extended across part of what is now modern day Belarus, Ukraine, Moldova, and Russia. The event caused concerns about human health for those living in the area as well as the potential risks of using contaminated land for farming. Immediately following the disaster, emphasis was placed on risk from radiation exposure, initially acute radiation sickness (ARS) and later cancer. Radiation concentrations were tracked and studies addressed acute radiation effects in the immediate victims[1,2], leukemia and thyroid cancer among children and clean-up workers[3-8], and cancer rates for some sites in the general population (e.g., breast cancer)[9-11].

The epidemic of thyroid cancer in children that shortly followed the Chernobyl catastrophe was not expected and to this day is not fully explained[12,13]. Excesses of other cancers have not been detected with the exceptions of leukemia in liquidators and premenopausal breast cancer in women in the general population[14-16]. Twenty-eight (28) years after the event, possible health effects other than cancer have not been fully addressed. Psychological effects including anxiety, depression, suicide, Post-Traumatic Stress Disorder (PTSD) and diminished overall well-being are among the principal concerns for Chernobyl survivors at present. Non-cancer effects including cardiovascular disease (CVD), respiratory diseases, immune function and other blood-related disorders, and reproductive health are also affecting those who were in the area at the time of the disaster and those who continue to reside in areas contaminated by the fallout.

Various summary reports and publications by the World Health Organization (WHO) and the International Atomic Energy Agency[14-16] as well as systematic reviews by Bromet, Havenaar, and Guey[17] and our own reports completed in 2011 and 2013 for Green Cross Switzerland[18,19] reached similar conclusions as to the lack of studies on non-cancer health effects.

The world experienced another disaster involving a nuclear power plant on March 11, 2011 when the Fukushima Daiichi Nuclear Power Plant failed following an earthquake and tsunami. There, an estimated 140,000 people were evacuated, and over 100,000 were still displaced by the end of 2013[20,21]. The same issues that were experienced by Chernobyl-exposed populations are now a concern in Japan[22-24], strengthening the need for more research on the long-term non-cancer effects of nuclear power plant accidents.

Psychological and Psychiatric Consequences of the Disaster

Apart from the radiation exposure, those living in the areas around the site experienced various acute and chronic stressors. These stressors have documented potential to affect quality of life and lead to psychological and psychiatric disorders among the survivors. Examples of such stressors include those following directly from the disaster with the potential for leading to PTSD, widespread displacement because of contamination, concern about future risks of disease, and even stigmatization as a group viewed as damaged by the disaster.

The WHO report on the health effects of the Chernobyl disaster characterized the "mental health impact" as "…the largest public health problem caused by the accident to date"[16 (pg95)]. A previous systematic review in 2007 by Bromet and Havenaar[25] only identified four (4) surveys that met inclusion criteria. Both this review and the Bromet and colleagues[17] review in 2011 called for more studies on Chernobyl liquidators (clean-up workers). Our previous reviews concluded that individuals affected by the Chernobyl accident "…have sustained neuropsychological consequences and these consequences remain of public health and medical significance". This present report updates the 2011 and 2013 reviews that we conducted in order to have the most complete picture possible of the evidence on consequences of the Chernobyl disaster with reference to neuropsychological and non-cancer outcomes. We have augmented the prior reviews with greater attention to the "grey literature" and the non-English language literature.

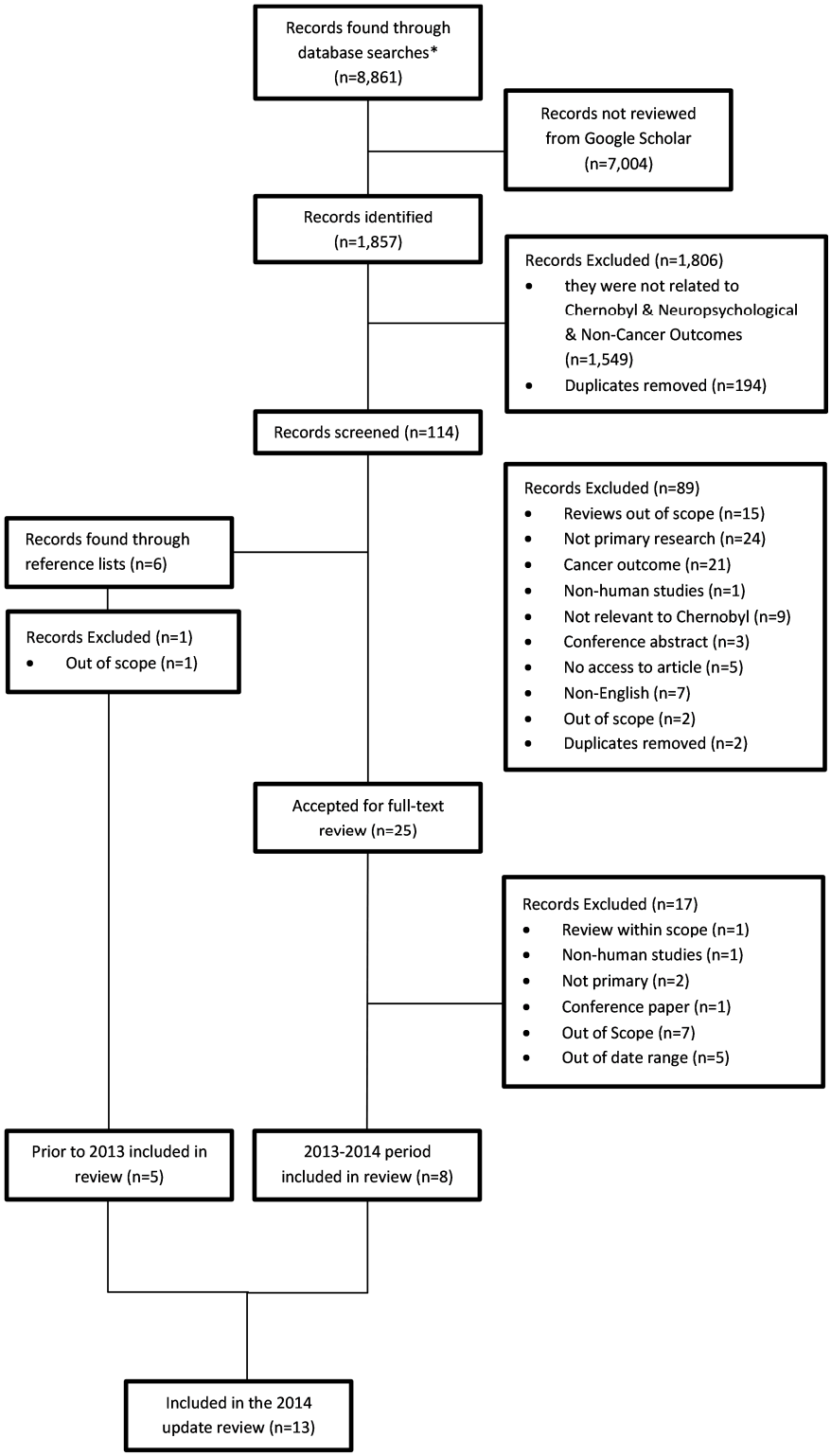
METHODS

To document in depth any progress in the literature and the current state of the evidence on the neuropsychological consequences (i.e., quality of life, functioning, morbidity/life expectancy, anxiety, depression, PTSD, well-being, and cognition) and non-cancer effects (i.e., suicide, reproductive health, CVD, immune function and other blood-related disorders, and respiratory diseases) related to the Chernobyl accident, we carried out an update of our previous systematic reviews of the literature[18,19]. To do so, we carried out multiple searches including: 1) an update to the English language literature from February 2013, the cut-off date for the prior search, through January 2014, 2) separate searches for non-English literature spanning to January 2014, and 3) searches for relevant "grey literature". The update to the English literature included over 1,500 new publications that were screened to identify relevant studies. In addition, we checked the references of relevant sources and other reviews on the subject to find relevant papers, including those published prior to 2013 to ensure that relevant articles were not missed. Keyword searches were conducted on PubMed, MEDLINE, Web of Knowledge, PAIS International via ProQuest, and PsycInfo. Additionally, USC Scholar Portal and Google Scholar were used to identify publications that were not in the usual scientific literature. The search strategies are presented in Table 1. Non-English publications were excluded in the initial search of this review because separate non-English searches were conducted for all years at a later stage of the literature search process. Only peer-reviewed publications were included as part of the review. For Google Scholar, only the first 60 results of each search, sorted by relevance, were reviewed because of the lack of specificity of this search engine, compared with the others used. Initially publication titles and summaries were scanned for relevance to Chernobyl, excluding publications about Fukushima and other nuclear power plants, and studies that were not about the populations affected by the accident. Duplicates were removed. The abstracts of one hundred fourteen (114) records were reviewed further to extract those publications relevant to neuropsychological consequences and non-cancer effects of the Chernobyl accident. Publications eliminated included reviews and other non-primary research, non-human studies, studies pertaining to cancer outcomes, conference abstracts and proceedings, publications found to be out of the scope of this review, any publication for which no full article could be obtained, and articles that were not in English. Twenty-five (25) publications were accepted for full-text review. Publications were read and data was abstracted using data abstraction forms created for this review. Authors

reviewed the publications to finalize inclusion of studies. If disagreements arose, these were resolved through discussion and Dr. Jonathan M. Samet made the final decision on inclusion of studies for this review. A PRISMA (Preferred Reporting Items for Systematic Reviews and Meta Analyses) diagram delineating steps taken during a systematic review process was used to summarize the exclusion of studies and articles at each stage of our process [26]. The PRISMA diagram for the review is presented in Figure 1. In total, 8 publications were published between February 1, 2013 and January 31, 2014 and met inclusion criteria for this update of the literature on the neuropsychological consequences and non-cancer effects of the Chernobyl accident. Additionally, 5 studies published prior to 2013 were found to be relevant that were not included in our previous reports. The studies were cited in the publications reviewed and the reference lists of reviews on the Chernobyl disaster. Two of these studies, Adams, R.E. and colleagues (2011) and Cwikel, J.G. and colleagues (2000), were additional reports on studies that we included in our reviews from 2011 and 2013. Results for these five additional studies are found in Appendix B and Table 11.

Separate searches of non-English literature and grey literature were also conducted. These searches included publications for all years through January 2014. Our team was initially unable to locate full text for the majority of the studies published in non-English journals; however, efforts to locate and translate these articles continue. Tables 19-27 list 328 publications that are potentially relevant to the focus of this report, for which we are currently attempting to gain access to the full text. Appendix C and tables 12-18 summarize the findings from 10 non-English publications for which we were able to find full text and translate when necessary. Eight (8) articles had English translations provided from the author(s), while 2 articles required translation. Google translate was utilized to translate the documents if the English abstracts provided by the authors could be used to ensure appropriate translation and understanding of the findings.

Figure 1. PRISMA Diagram for Study Selection: peer-reviewed, English language publications



RESULTS

Tables were constructed to highlight the main findings in the studies published since the prior reports. Each table includes studies for the different outcomes evaluated. The update for outcomes that were first examined in the 2011 report includes: anxiety, depression, PTSD, cognition, functioning, and well-being. In the 2013 report, non-cancer outcomes were evaluated in addition to the same neuropsychological consequences from the 2011 report. These outcomes include: suicide, CVD, reproductive health, immune function and other blood-related disorders, and respiratory diseases. No studies were found that met our criteria on the topics of reproductive health or immune function and other blood-related disorders. The studies focused on 3 main groups: 1) survivors of the Chernobyl disaster who were children at the time of the accident, 2) clean-up workers (liquidators), and 3) evacuees from the Chernobyl exclusion zone and those residing in highly contaminated areas. Control groups included the general population of the country being studied and nonexposed individuals matched for age, sex and factors relevant to the studies.

Table 2. Used Measurements includes a list of the scales and questionnaires used to assess psychological outcomes in each study. Appendix A lists each scale with its full name and its measurement objective. Two studies utilized various scales that have been widely used and are well documented. The study by Mykhaylov, V. and Zdesenko, I.[27] did not report the scales used to assess psychological disorders and only stated that clinical psychopathology was assessed (see Table 3 for highlights of the study findings). Overall trends pointed to worse scores in those exposed to the Chernobyl accident compared to those that were not exposed. The following are findings grouped by outcomes.

Neuropsychological Consequences

Three studies attempted to characterize the neuropsychological consequences of the Chernobyl accident (i.e., anxiety, depression, PTSD, cognition, and well-being). Table 3 provides details on these studies. All tables are organized alphabetically by first author's last name.

Masunaga, T. and colleagues[28] assessed well-being based on self-reported mental health status using a standard questionnaire. The cross-sectional study was conducted in Gomel, Belarus among 697 medical students at the Gomel State Medical University. Participants of the study were administered a questionnaire that included the General Health Questionnaire (GHQ-12). Participants were divided into two groups, those who scored 4 or more points on the GHQ-12 and those who scored under 4 points. Univariate analysis found significant differences between the high GHQ-12 score group and the low GHQ-12 score group for "not poor economic situation", "past medical history of CVD" and "association of diseases and/or poor health condition with radiation exposure" ($p<0.001$, $p=0.03$, and $p=0.003$, respectively). Multivariate analysis revealed that "not poor economic situation" and "association of diseases and/or poor health condition with radiation exposure" were still significantly associated with poor mental health, after adjusting for confounding factors (OR: 0.31, $p<0.01$ and OR: 1.78, $p<0.01$, respectively). Overall, the authors reported anxiety about radiation exposure as a factor affecting the poor mental health of participants[28]. Cautious interpretation of the findings is needed because the study is cross-sectional and Chernobyl-related exposures were not assessed in-depth.

Two studies focused on anxiety, depression and/or PTSD. The study conducted by Mykhaylov, V. and Zdesenko, I.[27] aimed at understanding the structure and dynamics of psychological disorders in 300 patients who were liquidators of the Chernobyl disaster, although its methods were not well documented. Patients were followed in four stages from 1986 to 2013. At stage one (1986-1989), patients fell into 3 categories: 53% had "vegetative-vascular" (the term is equivalent to "other disorders of autonomic nervous system" in the ICD-10), 41% had chronic cerebral ischemia, and 6% had acute cerebral circulation disorders. Additionally, several clinical syndromes were also reported to be present, including asthenia (86%), neurasthenic syndrome (14%), "liquor hypertension"—the authors' terminology—(37.6%), vestibular syndrome (16.8%), and paroxysmal syndrome (54%). A break in disease progression was noted at the time of first follow-up; however, by follow-up stage three (1994-1999) patients were presenting with hypochondria (18%), sub-depression (17.9%), obsession (6.9%), and hysteria (17.1%). The authors reported asthenic syndrome progressing from "physiogenic" to "psychogenic". During the fourth stage (2000-present), Mykhaylov, V. and Zdesenko, I.[27] found that disease had increased in what they called "organic" processes, while neurotic disorders had decreased. The team reported an increase in hypertension to 47% of patients, cerebral atherosclerosis in 23% of patients and cerebral strokes in 12% of patients. Additionally, they reported the development of encephalopathy in 69% of patients, which they defined as a disorder "with its neurologic and psychic deficits and specific morpho-functional cerebral changes"[27]. Because the methods are not presented with transparency and the syndromes are not explicitly defined, interpretation of these findings needs to be guarded.

Loganovsky, K.N. and Zdanevich, N.A.[29] also addressed psychological consequences in a study of 241 Ukrainians using a battery of psychometric scales and quantitative electroencephalography (qEEG). The participants included Chernobyl clean-up workers with PTSD, some of whom had Acute Radiation Sickness (ARS), and also Afghan war veterans with PTSD. Methods are described only briefly. In this cross-sectional study, Chernobyl survivors with PTSD (clean-up workers and evacuees) had, by far, more pronounced levels of psychological disorders compared to veterans of war and healthy persons. Their trait and state anxiety, as well as the cerebral hemodynamics disorders, neurologic deficit and cognitive impairment were more pronounced compared to control groups (veterans and healthy persons). Within Chernobyl clean-up workers, those without ARS had higher state anxiety compared to those with ARS. Depression was also higher for all Chernobyl survivors with PTSD compared to veterans and healthy persons. The greatest severity of post-radiation PTSD was seen in Chernobyl clean-up workers without ARS and evacuees. In terms of psychopathology, Chernobyl clean-up workers (both with ARS and without) showed higher levels compared to evacuees ($p<0.01$ and $p<0.05$, respectively), veterans ($p<0.001$ and $p<0.001$, respectively), and healthy persons ($p<0.001$ and $p<0.001$, respectively). PTSD was also higher for Chernobyl survivors, with Chernobyl clean-up workers without ARS showing higher indices of PTSD. Clean-up workers without ARS assessed their health as worse in comparison to those with ARS, evacuees and control groups. Chernobyl survivors also differed significantly from control groups in the rates of radiation-associated and social stress, subjective sense of time-space compression, hypochondria and somatization, learned helplessness, and depression. Also noted was the decreased level of memory, attention and verbal retroactive inference in clean-up workers with ARS, and auditory-verbal memorization, proactive verbal inference and short-term verbal memory in all

clean-up workers. Quantitative EEG (qEEG) showed a reduction in spectral power of beta activity for all patients with PTSD, especially clean-up workers with ARS. The investigators also found that all Chernobyl survivors with PTSD had decreased theta-power and increased alpha-power compared to war veterans.

Loganovsky, K.N. and Zdanevich, N.A.[29] characterized cerebrovascular disease in patients exposed to Chernobyl radiation by measuring, via ultrasound scans, the intima-media thickness of the cerebral and neck vessels. The study found the thickness of the complex intima-media in the common carotid arteries to be largest (mean 1.2 SD ±0.2mm) in Chernobyl clean-up workers from the Ukraine compared to veterans of the Afghanistan war and healthy controls ($p<0.05$). Indicators of a stenosis of the left internal carotid artery were highest among clean-up workers with past ARS (3.2 ±10.4) among all Chernobyl survivors (clean-up workers with ARS, clean-up workers without ARS and evacuees) ($p<0.05$). Likewise, rates of stenosis in the left common carotid artery were found to be higher in clean-up workers with ARS (12.0 ±19.2) compared to evacuees (4.6 ±13.3, $p<0.05$) and veterans of war (2.0 ±10.4, $p<0.02$). Incidence of right common carotid artery stenosis was highest among clean-up workers with ARS (18.4 ±22.1) compared with those without ARS (9.1±180, $p<0.05$), evacuees (4.7 ±12.5, $p<0.001$), veterans (6.3 ±150, $p<0.05$)[29].

Suicide

Previous studies have found that suicide rates are higher in countries most affected by the Chernobyl accident[30,31]. Using data for Belarus, Grigoriev, P. and colleagues[32] examined mortality rates for 1997-2007 using age-standardized death rates (SDR)—age specific rates were calculated for a 5-year period and a 3-year period at the rayon and oblast levels, respectively and were then standardized using the European population standard—and found that deaths from external causes (e.g., suicide, poisoning, and homicide) were the second leading cause of mortality in the country[1]. The study was not specific to the effects of Chernobyl, rather it examined overall mortality and cause-specific mortality in the country. The Chernobyl disaster impacted some areas of Belarus more than others. To understand if mortality patterns were different in areas with high levels of contamination, Grigoriev, P. and colleagues constructed mortality maps. Their findings showed that high levels of mortality from the selected causes of the study were found in areas highly affected by Chernobyl (Mogilev and Gomel oblasts); however, they reported that the "impact [of radiation from Chernobyl] does not appear to be very pronounced or conclusively established" [32]. For suicide, SDR for males and females in Belarus between 2005 and 2007 were calculated at 50.3 and 7.5 per 100,000 population, respectively. In recent years, mortality due to external causes declined in the country and varied by region, with reported SDR for men that varied from 183 in Minsk-city to 318 in Vitebsk per 100,000 population, while for women, the SDR ranged from 42 in Minsk-city to 78 in Vitebsk between 2005 and 2007. Rahu, K. and colleagues[33] used the Estonian Causes of Death Registry along with other sources to examine Estonian clean-up workers' mortality rates (using standardized mortality ratios- SMR) and compared the rates with those for the Estonian general male population. This update of 4,810 participants, continue to find excess mortality for suicide in Estonian clean-up workers compared to the general male population in Estonia (SMR 1.30, 95% CI: 1.05-1.60). The authors reported that the observed excess risk was not diminished from their previous

[1] The study by Grigoriev, P. et al. was published online in 2012 and was included in our 2013 report.

report (SMR 1.30 from 1986-2011 vs SMR 1.32 from 1986-2002). When coupled with undetermined injury, the point estimate was slightly lower (SMR 1.24, 95% CI: 1.01-1.47).

Cardiovascular disease

Five studies addressed CVD outcomes and the Chernobyl disaster. Table 5 highlights the findings of these cross-sectional and cohort studies. CVD was assessed with various indicators, including cause-specific mortality rates, hypertension and cerebral stroke, clinical and biochemical parameters—including carotid diameter, carotid-intima-media thickness (IMT), distensibility and stiffness—and conducting peripheral blood testing for cell counts and blood plasma. Study populations varied in terms of country and age group.

The study by Grigoriev, P. and colleagues[32] also found that in Belarus, mortality due to CVD accounted for more than half of deaths in the country. While the authors could not establish the effect of the Chernobyl disaster on the cause-specific death rates, SDR attributed to diseases of the circulatory system were calculated at 1,033 and 592 for men and women per 100,000 population for the years 2005-2007, respectively. The lowest SDR by heart disease was observed in the capital, where 558 deaths in men and 269 deaths in women were caused by CVD per 100,000 population; while the highest mortality for CVD was found in the central and eastern parts of Belarus. While the overall trend of mortality in Belarus had been increasing for CVD prior to the 2000s, Grigoriev, P. and colleagues[32] report a decreasing trend since then.

Bruno, R.M. and colleagues[34] conducted a cross-sectional study of 46 participants, including 23 designated as exposed and 23 as non-exposed controls, who were 8 years old or younger at the time of the Chernobyl accident. The aim was to understand the pro-atherosclerotic effects of radiation exposure in Chernobyl survivors by conducting measurements and collecting blood samples. Examining Belarusian males and females— those exposed to radiation and subsequently diagnosed with papillary thyroid cancer and treated with radioiodine ablation in comparison with non-exposed controls matched on sex, age and cardiovascular risk factors—the study found that the two groups did not differ in terms of carotid diameter, IMT, distensibility and stiffness, and carotid-femoral pulse wave velocity. However, pulse pressure amplifications from carotid to brachial site was significantly higher in exposed subjects compared to non-exposed after adjusting for covariates ($p=0.04$). Response to glyceryl trinitrate and carotid augmentation index normalized at 75 bpm (carotid AIx) were both higher in exposed subjects ($p=0.01$ and $p=0.02$, respectively) compared to non-exposed[34]. The most significant difference reported by the authors between the two groups was the reduced number of endothelial progenitor cells (EPCs) ($CD34^+KDR^+$, $CD34^+$ $CD133^+$, $CD34^+$ $CD133^+$ KDR^+) in exposed versus non-exposed ($p<0.0001$ for all). The findings need to be interpreted with consideration of the small sample size and the highly selected participants.

Another study indirectly concerning CVD was conducted in the Ukraine between 2009 and 2013[35]. In this study, Mishcheniuk, O.Y. and colleagues[35] aimed at understanding how gene mutations (JAK2V617F) or other coexisting thrombophilic risk factors contributed to thrombotic complications in patients with Ph-negative myeloproliferative neoplasms (MPN) who were exposed to Chernobyl radiation compared to patients with sporadic Ph-negative MPN. While the study did not find significant

differences between the exposed and non-exposed in terms of clinical parameters, it did find that a trend of primary myelofibrosis (PMF) patients with allele frequency of G1691A allele factor V gene polymorphism was significantly higher in patients with thrombosis than those without thrombotic episodes (p=0.03). The trend was also seen in those PMF patients exposed, but it was not observed in those non-exposed. Among those exposed to Chernobyl radiation, Mishcheniuk, O.Y. and colleagues[35] report a higher prevalence of the G1691A allele of factor V and/or G20210A allele of prothrombin gene among exposed patients with thrombosis compared to exposed patients without thrombosis (3 of 13 vs. 0 of 32 patients, p=0.02).

Evaluating plasma albumin alterations in Latvia's male Chernobyl clean-up workers with type 2 diabetes mellitus compared to non-diabetic and healthy controls, Kalnina, I. and colleagues[36] found that the average fluorescence intensity of ABM in blood plasma —the 3-aminobenzanthrone derivative synthesized at Daugavpils University, Daugavpils, Latvia, which the authors describe as a probe for albumin alterations—was significantly higher in all Chernobyl groups compared to healthy donors. Fluorescence intensity was recorded and reported in arbitrary units, F(AU), calculated as F(AU) 3.56±0.07 for clean-up workers with diabetes mellitus, F(AU) 3.13±0.06 clean-up workers with diabetes mellitus and CVD, F(AU) 2.58±0.07 clean-up workers without diabetes mellitus and F(AU) 2.11±0.06 in controls, corresponding to increases of 68.7%, 48.3%, and 22.3% (Note that the authors mistakenly report 35.1%) for groups 1, 2 and 3 compared to controls, respectively. Per the authors' description, dehydration of the tryptophanyl region was more pronounced in the Chernobyl clean-up workers with diabetes mellitus compared to the other groups. According to the authors, this translates to rigidity of the tryptophanyl region. For albumin auto-fluorescence, Kalnina, I. and colleagues[36] found a shift from fluorescence zone to short-wave region coupled with a decrease in fluorescence intensity. They concluded that this was evidence of "a more significant hydration process in the albumin tryptophanyl region in diabetics (groups 1 and 2) as compared with group 3 and the control group"[36]. Diabetics had a more significant hydration process in the albumin tryptophanyl region (only diabetes mellitus: F(AU) = 0.87 ± 0.05 and diabetes mellitus and CVD: F(AU)=1.01 ±0.05) compared to non-diabetics (F(AU)=1.85 ± 0.06) and controls (F(AU)=2.96 ±0.05)[36]. Lastly, Kalnina, I. and colleagues[36] evaluated the ABM binding with plasma albumin and found the Effective Albumin concentrations in Chernobyl survivors to decrease, "providing a basis for the development of various diabetic complications". Effective Albumin concentrations decreased in those with diabetes mellitus, those with diabetes mellitus and CVD, and those without diabetes mellitus by 51.8%, 44%, and 26.8%, respectively. There was a significant difference between all groups based on reserve of albumin binding capacity (**E**ffective **A**lbumin concentration/**T**otal **A**lbumin concentration). Chernobyl clean-up workers with diabetes had the lowest albumin binding capacity at 0.45±0.03 compared to the control group at 0.81±0.04[36]. The study employed a non-standard methodology—the ABM—that is not routinely used in clinical medicine and poorly documented, and study findings should be regarded with caution.

Ukrainian men in the study by Mykhaylov, V. and Zdesenko, I.[27] presented with neurologic and cerebrovascular disorders, which 8 years later (at stage 3 and 4 of the study) included cardiovascular diseases, including hypertension. In stage 3 they found that "cognitive deficiency syndrome", hypertension and cerebral atherosclerosis were present in 38%, 27% and 5% of patients, respectively. In

the latest stage (2000-present), Mykhaylov, V. and Zdesenko, I. reported an increase in hypertension and cerebral atherosclerosis (47% and 23%, respectively), presence of cerebral stroke (12%) and development of encephalopathy in 69% of patients[27].

Respiratory disease

Two studies, one by Grigoriev, P. and colleagues[32] and the other by Rahu, K. and colleagues[33], explored outcomes of respiratory disease in relation to Chernobyl exposure. Mortality rates for the disease were used as indicators of the impact from the Chernobyl accident. Grigoriev. P. and colleagues did not find respiratory diseases to be a main cause of death in Belarus; however these diseases influenced the variation in mortality at the regional level (inter-regional mortality)[32]. The study found two regions, the Vitebsk and Grodno oblasts, to have much higher mortality due to respiratory diseases than other oblasts, where SDR for men were calculated at 167 and 152, and for women at 32 in each oblast per 100,000 population, respectively. These findings were not linked to the Chernobyl accident, but help understand the overall health of the population in an area highly affected by the accident. A high mortality cluster from respiratory disease was apparent in the northern part of the country[32]. Similar to the study in Belarus, Rahu, K. and colleagues[33] studied mortality rates in Estonia. Compared to the Estonia general male population, Estonia clean-up workers did not have significantly higher mortality rates due to respiratory diseases[33].

Immune function and other blood-related disorders

Our previous report[19] concluded that taken together, the studies focusing on immune function and other blood-related disorders identified associations with the Chernobyl disaster, but the underlying mechanisms were not clear. To the authors' knowledge, no studies, in English, on immune function and other blood-related disorders in relation to the Chernobyl disaster were conducted during the period of this update to the review.

DISCUSSION

This report provides an update of the literature for selected health consequences of the Chernobyl disaster and expands on our two previous reviews (see Table 7, Table 8, and Table 9 for summary of findings from the 2011, 2013 and 2014 reports, respectively). We identified 8 new reports providing relevant information and an additional 5 studies prior to 2013. Studies have shown persistent neuropsychological consequences and non-cancer effects related to the Chernobyl accident[17,37-48]. Based on studies conducted in various populations and in different areas affected by Chernobyl, our previous reviews concluded that individuals affected by the Chernobyl accident "…have sustained neuropsychological consequences and these consequences remain of public health and medical significance" [18,19]. The newer evidence further supports this conclusion.

Neuropsychological Consequences

The neuropsychological consequences of the Chernobyl disaster range from anxiety to PTSD and depression. Our first report covering the topic[18] found persistent neuropsychological consequences in the populations affected by the disaster. The findings were in accordance with other reviews and

supported by our focus group findings[17,49]. This update included three new studies addressing the topic. Findings from these studies indicate that the Chernobyl disaster affected survivors, even those born after the accident. Masunaga, T. and colleagues[28] concluded that the younger generation suffers from an imprinted victim consciousness, and that radiation health risk communication is necessary to avoid misunderstanding and reduce anxiety. Mykhaylov, V. and Zdesenko, I.[27] found survivors to be suffering from anxiety and disorders of the nervous system. Over time, physiological deterioration was present including higher prevalence of hypertension and cerebral atherosclerosis. Furthermore, Loganovsky, K.N. and Zdanevich, N.A.[29] found that those with PTSD due to exposure to the Chernobyl accident had more severe psychopathology than war veterans with PTSD and healthy adults. Loganovsky's group also found that clean-up workers had more pronounced neurological disorders, such as impaired memory and attention. Additionally, these individuals were at a higher risk for cerebrovascular disorders, including stroke[29]. The literature in this topic continues to confirm that the Chernobyl accident not only caused radiation sickness and cancer, but long-term neuropsychological consequences that continue to reduce the quality of life of survivors and younger generations.

Reproductive health

Our previous reports found a consistent drop in birth rates—following the disaster—across studies, and in general, "…the degree of maternal stress extended from those living at distances from the site with general concerns about their children to those who lived nearby and were forced to relocate"[19]. We did not find new studies that were conducted during the period of this review, reported in English, and focusing on reproductive health in relation to the Chernobyl accident.

Suicide

Studies addressing suicide (by exploring suicide rates, and change over time and location etc.) were inconclusive. Some found that Eastern European countries that were most affected by the Chernobyl accident had high suicide rates[30,31], while others found mixed evidence[50]. New studies in this report found external causes (including suicide) to be the second leading cause of death in Belarus; however, trends show a decline[32]. The study from Estonia continued to find an excess in suicide mortality rates, but reported that the excess did not change from their previous findings [33].

Cardiovascular disease

Among other causes, stress and PTSD have been linked to unfavorable cardiovascular risk[51-53]. For this reason, we evaluated the literature on the relationship between CVD and the Chernobyl accident. Our previous report found nine publications that addressed CVD. Based on these studies, we concluded that while they provided an indication of increased risk, the findings had to be interpreted with caution because the details of the methodology were lacking for a few studies, studies did not account for confounding, and the sensitive and more modern methods of investigation were not used[19].

This update found five more studies addressing the issue of CVD and Chernobyl exposure. Studies identified utilized mortality, genetics, arterial measurements, blood plasma and clinical risk factors (e.g., hypertension and stroke) as indicators of CVD. Kalnina, I. and colleagues' data suggest that the ABM probe, a non-standard method in clinical medicine, can be used as a biomarker of modified

albumin for patients with complex metabolic conditions to help identify individual who have a higher risk of suffering from CVD[36]. In their study, Kalnina, I. and colleagues[36] found significant changes in ABM fluorescence associated with plasma albumin in Chernobyl clean-up workers. Chernobyl clean-up workers with diabetes mellitus had more pronounced differences in parameters compared to Chernobyl clean-up workers without diabetes and healthy controls. The authors suggest that the biomarker findings have implications for the severity of the disease, but to our knowledge, this marker has not been validated. Grigoriev, P. and colleagues[32] found high CVD mortality rates in Belarus, but could not attribute the increments solely to the Chernobyl accident. Mishcheniuk, O.Y. and colleagues[35] concluded that inherited thrombophilia was an important risk factor in thrombosis for PMF patients, especially those exposed to Chernobyl radiation. Furthermore, Bruno, R.M. and colleagues[34] found that a reduced endothelial regeneration and repair capacity was seen in exposed subjects, and this could lead to an impaired endothelial response when vascular injuries resulted from aging. While they felt this alteration may not affect the young subjects, it may be relevant in later years, and place these subjects at a higher risk of developing cardiovascular complications[34]. Lastly, Mykhaylov, V. and Zdesenko, I.[27] observed a development of CVD among their cohort of patients, where prevalence of hypertension developed and increased with time. These findings, however, must be interpreted with caution due to the lack of details provided on methodology and non-standard approaches. Together these studies address a wide variety of CVD outcomes, but do not provide a cohesive body of evidence, given the heterogeneity of measures and inherent limitations of the studies.

Respiratory disease

The lack of studies addressing complications from respiratory disease due to Chernobyl exposure limits us from reaching any conclusions. Our previous report[19] found two studies. One indicated no direct pathways for the disaster to affect respiratory function and causing major respiratory disease, and another found that high levels of Cs-137 were associated with lung function abnormalities[42,47]. In this review, the two additional studies that focused on respiratory disease involved understanding mortality in general in Belarus[32], and in Estonia clean-up workers[33]. Grigoriev, P. and colleagues[32] found mortality due to respiratory disease to vary across Belarus; however, overall, it was not a major cause of death among Belarusians. Rahu, K. and colleagues[33] did not find a statistical difference in the mortality of Estonian clean-up workers due to respiratory disease compared to that of Estonia's male general population. Any conclusion on the possible causal effects of Chernobyl on respiratory disease cannot be determined unless further studies are conducted to understand how exposure to ionizing radiation from the Chernobyl catastrophe affected survivors.

Immune function and other blood-related disorders

Our previous report[19] concluded that the studies found suggested "the disaster may have affected the immune function but through unclear mechanisms". To the best of our knowledge, no studies were conducted during the period of this review, in English, focusing on immune function and other blood-related disorders in relation to the Chernobyl accident.

Limitations

Although the studies were included in the peer-reviewed literature, we identified a number of limitations that affected interpretation of the individual studies as well as integration of the findings overall. We found inadequate or confusing documentation of methods, small studies, and a reliance on cross-sectional approaches. We provide more in-depth comments in relation to particular reports in the results section of this review.

CONCLUSIONS AND RECOMMENDATIONS

Summary

The underlying intent of the authors of these papers was to generate evidence that will prepare and help survivors of the Chernobyl disaster to continue to live with a unique set of conditions brought on or exacerbated by experiences related to the Chernobyl disaster, and where possible, increasing their quality of life. Along with studies of specific outcomes, some investigators evaluated cause-specific and overall mortality for countries highly affected by the Chernobyl accident. Grigoriev, P. and colleagues[32] used data from the National Committee of Statistics in Belarus to examine SDR between 1997 and 2007 for overall and cause-specific mortality. Findings from this study showed that in Belarus, overall mortality tended to be higher in the eastern part of the country compared to the western part (an increase in SDR by 141 deaths among males and 78 deaths among females or by 7% and 8.5% of the average mortality level, respectively). Additionally, they found clusters from selected causes of death located in the Mogilev and Gomel oblasts, both areas highly contaminated by the Chernobyl accident. Grigoriev, P. and colleagues[32] could not confirm that these clusters were in fact caused by the accident, but they also could not discount the fact that they were in close proximity and their appearance was not a coincidence. Rahu, K. and colleagues[33] found that the risk of death rose significantly after 7 years since return from the mission to Chernobyl. Numerous studies are required to gain a deeper understanding of the effect the Chernobyl accident has had on mortality. The accident was not only responsible for acute radiation sickness and cancer, but left lasting non-cancer effects and neuropsychological consequences that further diminished the quality of life and mortality of the populations affected.

Together, the studies from our previous reports and the present report attest to the array of health issues burdening survivors of the Chernobyl disaster, from being displaced and exposed to varying levels of radiation. The English-language literature on neuropsychological consequences confirms that the Chernobyl accident continues to reduce the quality of life of survivors and also the indirectly affected younger generations. In our previous reports we called for more studies to be conducted on these non-cancer outcomes, especially CVD. The current literature indicates that survivors continue to have adverse consequences, and their struggle is far from over. More research on non-communicable diseases is needed that employs standard methodology. Research that meets our inclusion criteria has not yet reached to populations in Moldova. In the wake of the 2011 Fukushima disaster we must continue to conduct these studies, to help Chernobyl survivors and prepare for the lasting consequences that will become evident for this new set of victims of the Fukushima nuclear power plant accident.

Recommendations

Recommendations from the two earlier reports are summarized in Table 10. These recommendations covered various research and related policy needs. The findings of the additional studies reviewed here provide no basis for modifying these earlier recommendations. They continue to reinforce the need for studies that adequately address non-communicable diseases in light of the Chernobyl disaster.

TABLES AND APPENDICES

Table 1. Search Strategies in Conjunction with "Chernobyl" and "Chornobyl"

Topic	Search Words
Quality of Life	disaster life quality
Neuropsychological	disaster neuropsychological
Morbidity	morbidity
Function	functioning
Life Expectancy	disaster life expectancy
Anxiety/ Depression/ PTSD/ Cognition	anxiety OR depression OR PTSD OR post-traumatic stress disorder OR cognition
Well-Being	well-being
Suicide	ideation OR suicidal OR suicide OR suicides OR (suicide AND death) OR (suicides AND death) OR (suicide AND mortality) OR (suicides AND mortality)
Reproductive Health	abortion OR birth malformations OR congenital effect OR fetal death OR induced abortion OR infant death OR perinatal mortality OR pregnancy OR (reproductive AND health) OR reproductive health OR spontaneous abortion OR (still AND birth) OR stillbirth
CVD	Aneurysm OR atherosclerosis OR (blood AND circulation) OR blood circulation OR (cardiovascular AND diseases) OR (cardiovascular AND disorders) OR cardiovascular diseases OR cardiovascular disorders OR cardiovascular morbidity OR cardiovascular mortality OR cardiovascular system OR cerebrovascular OR (circulatory AND disease) OR circulatory disease OR coronary OR CVD OR electrocardiography OR heart OR (heart AND death) OR (heart AND disease) OR heart disease OR heart morbidity OR hypertension OR ischemic OR stroke OR Chest OR chest pain
Immune and Other Blood Disorders	immune function OR immune system OR immune system processes OR immunology
Respiratory Disease	lung OR (lung AND disease) OR lung disease OR pulmonary OR (pulmonary AND disease) OR pulmonary disease OR respiration OR respiration disorders OR respiratory disease OR respiratory disorders OR respiratory tract OR respiratory tract infections OR thorax

Table 2. Used Measurements

Study By Principal Investigator	Population Type	Measured Scales *				
		Anxiety	Depression	PTSD**	Well-Being	Cognition
Masunaga, T.	Medical Students	GHQ-12			GHQ-12	
Loganovsky, K.N.	Adults	BPRS, Spilberger-Khainin anxiety scale, IDA	BPRS, SDS, IDA	IDA, IES, IES-R, Mississippi PTSD Scale, "Radiation" PTSD questionnaire	BPRS, GHQ-28, FSS, EDSS, Ultrasound scans of cerebral and neck vessels	RAVLT, SKT, quantitative EEG (qEEG)
Mykhaylov, V.			Clinical psychopathological, instrumental and biochemical methods		Clinical psychopathological, instrumental and biochemical methods	
*Names of acronyms can be found in Appendix A						
**Post-Traumatic Stress Disorder						

Table 3. Literature Review: Findings on Neuropsychological Consequences (2011 review update)

Findings on Neuropsychological Consequences				
Reference	Source Description	Country, Period, Sex	Size (N), Type, Age (yrs)	Results
Grigoriev, P., et al.	Data from the National Committee of Statistics of Belarus were examined and Age-standardized Death Rates (SDR) were calculated. The study aimed at identifying temporal changes in overall and cause-specific mortality, compare areas contaminated due to Chernobyl with the rest of the country and link mortality to socio-economic indicators across regions.	Belarus, 1997-2007, Males & Females	Cross-sectional study of people in Belarus.	Mortality trend= higher in the Eastern part of the country than the Western part. Mortality trends= slightly more pronounced in women than men. Located in the Eastern part of Belarus is associated with an increase in SDR by 141 deaths among males and 78 deaths among females. Clusters for highest mortality from selected causes of death are located in the Mogilev or Gomel oblasts.
Loganovsky, K.N. and Zdanevich, N.A.	Patients were evaluated using the following psychometric scales: • Brief Psychiatric Rating Scale (BPRS) • General Health Questionnaire (GHQ-28) • Zung Self-Rating Depression Scale (SDS) • Spilberger-Khainin anxiety scale • Post-Traumatic Stress Disorder (PTSD) scales Irritability, Depression, Anxiety (IDA) • Impact of Events Scale (IES and IES-R) • Mississippi PTSD Scale	Ukraine; Males & Females	Cross-sectional study of 241 patients divided into four groups: 1)Chernobyl clean-up workers with PTSD (with Acute Radiation Sickness [ARS] and without ARS), 2) Chernobyl evacuees, 3) veteran of the Afghanistan war and 4) healthy persons never exposed to ionizing radiation; 36-	The Spilberger-Khainin anxiety scale test showed that all Chernobyl survivors with PTSD had more pronounced trait and state anxiety compared to war veterans and healthy controls. State anxiety was higher in Chernobyl Nuclear Power Plant (CNPP) clean-up workers without ARS than in those with ARS. Trait anxiety was higher in CNPP clean-up workers without ARS and evacuees than war veterans and healthy controls. From SDS scale: Depression in all CNPP clean-up workers (with and without ARS) and Chernobyl evacuees was more pronounced than in war veterans or healthy controls. PTSD in CNPP clean-up workers is

	• "Radiation" PTSD questionnaire developed by author and team Neurometric evaluation: • Functional System Scale (FSS) • Expanded Disability Status Scale (EDSS) Cognitive Functions: • Rey Auditory Verbal Learning Test (RAVLT) • Short Cognitive Performance Test (SKT) Neurophysiologic studies: • 16-channel quantitative electroencephalography (qEEG) with brain mapping of the main frequency ranges spectral analysis • Ultrasound scans of cerebral and neck vessels The study examined PTSD and other mental health disorders in Chernobyl Nuclear Power Plant (CNPP) clean-up workers with PTSD (with and without Acute Radiation Sickness [ARS]), and evacuees of Chernobyl exclusion zone with PTSD compared with Afghanistan veterans of war with PTSD and mild closed head		75 years old	characterized by the projection of fear and danger in the future ("flashforwards"). CNPP clean-up workers without ARS showed more pronounced indices of PTSD (assessed by IDA, IES, and Mississippi scale). Greatest severity of post-radiation PTSD was in CNPP clean-up workers without ARS and Chernobyl evacuees (assessed using the questions the group created called "Radiation" PTSD questionnaire). However, the lowest severity was seen in the CNPP clean-up workers who were diagnosed with ARS. All Chernobyl victims significantly differed from war veterans and healthy controls regarding increased rates of: 1) radiation-associated and social stress, 2) subjective sense of time-space compression, 3) hypochondria and somatization, 4) learned helplessness and 5) depression. Psychopathology (determined by BPRS) was higher in all CNPP clean-up workers than in Chernobyl evacuees, war veterans and healthy control groups. Self-assessment of health (GHQ-28) worst in CNPP clean-up workers without ARS than those with ARS, evacuees, war veterans and healthy control groups. Cognitive impairment was more pronounced in those affected by the Chernobyl disaster with PTSD than in war veterans and healthy controls. Memory and attention were worst in CNPP clean-up workers diagnosed with ARS (SKT scale)

	injury and a control group of health people not exposed to ionizing radiation.			Auditory-verbal memorization (RAVLT A1-A5), proactive verbal inference (RAVLT B) and short-term verbal memory (RAVLT A6) was worst in CNPP clean-up workers. Verbal retroactive inference (RAVLT A5-A6) was worst in CNPP clean-up workers with ARS. Neurologic deficit was more severe in Chernobyl survivors than war veterans and healthy controls. This is especially true for CNPP clean-up workers without ARS. Cerebral hemodynamics disorders were more pronounced in Chernobyl survivors with PTSD compared to war veterans and healthy controls. All patients with PTSD, especially CNPP clean-up workers with ARS had a reduction in the spectral power of beta activity of qEEG. Slowing EEG-pattern seen in war veterans could be due to mild closed had injury. Chernobyl survivors with PTSD had a decreased theta-power and increased alpha-power compared to war veterans.
Masunaga, T., et al.	Medical students were given a self-administered questionnaire including the General Health Questionnaire (GHQ-12). Participants were divided into two groups based on total GHQ-12 scores (high group ≥4 points and low group <4 points). The study examined the mental health status of medical	Gomel and other regions in Belarus and Russian Federation; Males & Females	Cross-sectional study of 697 medical students born after the accident attending Gomel State Medical University (Gomel, Belarus); 16-24 years old	Mean GHQ-12 score=1.80 ± 2.28 Comparisons for those with high GHQ-12 score and those with a low GHQ-12 score for: “Economic situation” p<0.001 “Past medical history of CVD” p=0.030 “Association of disease and/or poor health condition with radiation exposure” p=0.003 Associations with poor mental health: “Economic situation” = OR: 0.31, p<0.01

	students in Gomel, Belarus who were born after the Chernobyl accident.			"Association of diseases and/or poor health condition with radiation exposure"= OR: 1.778, p<0.01
Mykhaylov, V. and Zdesenko, I.	Clinical psychopathological, instrumental and biochemical methods were used to assess the clinical structure and dynamics of non-psychic psychic disorders within psychic-neurological disorders in persons exposed to radiation due to the Chernobyl accident. Patients who were exposed to Chernobyl radiation were evaluated and followed. An intervention that included medication, psychotherapy, and social therapy was developed. The exposed group was compared with a control group in terms of success of the rehabilitation program.	Ukraine, 1986-2013, Males	Prospective study of 300 adult patients, who were 30-45 years old in 1986	Patients were assessed at four stages: Stage #1(1986-1989): patients were identified in 3 groups: group 1 "Vegetative-Vascular"=53%, group 2 Chronic Cerebral Ischemia= 41%, and group 3 Acute Cerebral Circulation Disorders= 6%. Stage #2 (1990-1993): no changes were seen. Stage #3 (1994-1999): asthenic syndrome transitioned from physiogenic to psychogenic: Hypochondria=18%, Sub-depression= 17.9%, Obsession =6.9% and Hysteria=17.1%. Patients also presented with: Cognitive Deficiency Syndrome= 38%, Hypertension= 27% and Cerebral Atherosclerosis= 5%. Stage #4 (2000-present): increased "organic" processes with decreased neurotic disorders. Hypertension increased to 47% of patients as well as Cerebral Atherosclerosis to 23% and Cerebral Stroke to 12%. Encephalopathy developed in 69% of patients.
Rahu, K., et al.	Used the Estonian Causes of Death Registry and assessed risk of death from different causes by the standardized mortality ratio (SMR)-expressed as a ratio of observed to expected number of cases. Risk of death (mortality risk) was examined for Estonian Chernobyl Nuclear Power Plant (CNPP) clean-up	Estonia, 1986-2011, Males	The update of results was conducted on 4,810 adults.	The risk of death rose significantly after 7 years since return from Chernobyl, and stayed the same for those who stayed more than 14 years.

	workers cohort (assembled in 1992 from several data sources) compared to the Estonian male population.			

Table 4. Findings on Suicide (2013 review update)

Findings on suicide				
Reference	Source Description	Country, Period, Sex	Size (N), Type, Age (yrs)	Results
Grigoriev, P., et al.	Data from the National Committee of Statistics of Belarus were examined and Age-standardized Death Rates (SDR) were calculated. The study aimed at identifying temporal changes in overall and cause-specific mortality, compare areas contaminated due to Chernobyl with the rest of the country and link mortality to socio-economic indicators across regions.	Belarus, 1997-2007, Males & Females	Cross-sectional study of people in Belarus.	External cause was the second leading cause of death in Belarus. Suicide is among the categories of external cause. Over the last few years, mortality from external causes has been declining in Belarus. External cause mortality SDR for men varies from 183 (Minsk-city) to 318 (Vitebsk) per 100,000 population. Suicide SDR 2005-2007: • Men= 50.3 per 100,000 population • Women= 7.5 per 100,000 population
Rahu, K., et al.	Used the Estonian Causes of Death Registry and assessed risk of death from different causes by the Standardized Mortality Ratio (SMR)- expressed as a ratio of observed to expected number of cases. Risk of death (mortality risk) was examined for Estonian CNPP clean-up workers cohort (assembled in 1992 from several data sources) compared to the Estonian male population.	Estonia, 1986-2011, Males	The update of results was conducted on 4,810 adults.	Excess mortality for suicide SMR= 1.30, 95% CI: 1.05-1.60 Excess mortality for suicide combined with undetermined injury SMR= 1.24, 95% CI: 1.01-1.47

Table 5. Literature Review: Findings on Cardiovascular Disease (2013 review update)

Findings on CVD				
Reference	Source Description	Country, Period, Sex	Size (N), Type, Age (yrs)	Results
Bruno, R.M., et al.	Age, height, heart rate, carotid intima—media thickness assessment (CIMT), aortic and carotid stiffness measurement, and peripheral blood testing for endothelial progenitor cells (EPC) were collected. The study examined proatherosclerotic effects of radiation exposure in Chernobyl survivors. Participants were children at the time of the accident and were subsequently diagnosed with papillary thyroid cancer and treated with radioiodine ablation and were compared to non-exposed, matched controls (matched on age, sex and cardiovascular risk factors).	Belarus, Males & Females	Cross-sectional study of 46 participants who were 8 years old or younger at the time of the Chernobyl accident.	Groups (exposed vs. nonexposed) did not differ in terms of carotid diameter, CIMT, distensibility and stiffness, and carotid-femoral pulse wave velocity (PWV). Pulse pressure amplification from carotid to brachial site was significantly higher in exposed than nonexposed subjects after adjusting for covariates (p=0.04, controlling for age, height, and heart rate). Carotid augmentation index normalized at 75 bpm (Carotid AIx) was higher in exposed than in nonexposed subjects (p=0.02, unadjusted). Unadjusted response to glyceryl trinitrate (GTN) was significantly greater in exposed than in nonexposed (p=0.01, unadjusted). The number of Endothelial Progenitor Cells (EPCs) was significantly reduced in exposed compared to nonexposed subjects (p<0.0001).
Grigoriev, P., et al.	Data from the National Committee of Statistics of Belarus were examined and Age-standardized Death Rates (SDR) were calculated. The study aimed at identifying temporal changes in overall and cause-specific mortality, compare	Belarus, 1997-2007, Males & Females	Cross-sectional study of people in Belarus.	CVD mortality is responsible for more than half all deaths in Belarus. Total SDR for diseases of the circulatory system: • Men= 1,033 per 100, 000 population • Women= 592 per 100,000 population Lowest SDR by heart disease was seen in the capital: 558 deaths in

	areas contaminated due to Chernobyl with the rest of the country and link mortality to socio-economic indicators across regions.			men and 269 deaths in women per 100,000 population. Higher CVD mortality found in central and eastern parts of the country. CVD mortality increased until the 2000s. Trend is now decreasing.
Kalnina, I., et al.	Blood plasma was evaluated to understand plasma albumin alterations in Chernobyl Nuclear Power Plant (CNPP) clean-up workers with type 2 diabetes mellitus compared with CNPP clean-up workers that were non-diabetic and healthy controls, not professionally exposed to ionizing radiation.	Latvia, 2011, Males	Cross-sectional study	The average fluorescence intensity of ABM (3-aminobenzanthrone derivative) in blood plasma was significantly higher in Chernobyl groups F(AU)= 3.56±0.07, F(AU)= 3.13±0.06, F(AU)= 2.58±0.0, corresponding to an increase of 68.7%, 48.3%, and 22.3% (the authors' mistakenly reported 35.1%) for groups 1, 2, and 3, respectively compared to healthy donors F(AU)= 2.11±0.06. There is a more significant hydration process in the albumin tryptophanyl region in diabetics group 1 F(AU)= 0.87 ± 0.05 and group 2 F(AU)= 1.01 ±0.05 as compared to group 3 F(AU)= 1.85 ± 0.06 and controls F(AU)= 2.96 ±0.05. ABM binding with plasma albumin: Effective Albumin concentration for patients in groups 1, 2, and 3: F(AU)= 32.8±2.1, F(AU)= 38.1±1.8, F(AU)= 49.8±2.6, compared to control, F(AU)= 68.0±3.4. Reserve of Albumin binding capacity: group 1 F(AU)= 0.45 ±0.03, group2 F (AU)= 0.53±0.02, group 3 F(AU)= 0.66±0.03, and control F(AU)= 0.81±0.04.

Loganovsky, K.N. and Zdanevich, N.A.	Patients were evaluated using the following psychometric scales: • Brief Psychiatric Rating Scale (BPRS) • General Health Questionnaire (GHQ-28) • Zung Self-Rating Depression Scale (SDS) • Spilberger-Khainin anxiety scale • Post-Traumatic Stress Disorder (PTSD) scales Irritability, Depression, Anxiety (IDA) • Impact of Events Scale (IES and IES-R) • Mississippi PTSD Scale • "Radiation" PTSD questionnaire developed by author and team Neurometric evaluation: • Functional System Scale (FSS) • Expanded Disability Status Scale (EDSS) Cognitive Functions: • Rey Auditory Verbal Learning Test (RAVLT) • Short Cognitive Performance Test (SKT) Neurophysiologic studies: • 16-channel quantitative electroencephalography (qEEG) with	Ukraine; Males & Females	Cross-sectional study of 241 patients divided into four groups: 1)Chernobyl clean-up workers with PTSD (with Acute Radiation Sickness [ARS] and without ARS), 2) Chernobyl evacuees, 3) veteran of the Afghanistan war and 4) healthy persons never exposed to ionizing radiation; 36-75 years old	Thickness of complex intima-media in the common carotid arteries was largest (mean 1.2 SD ± 0.2mm) in clean-up workers ($p<0.05$) which may increase risk of stroke. Highest incidence of right common carotid artery stenosis were seen in clean-up workers with ARS (18.4 ±22.1) compared to CNPP clean-up workers without ARS (9.1 ±180, $p<0.05$), CNPP evacuees (4.7 ±12.5, $p<0.001$) and veterans (6.3 ±150, $p<0.05$). Higher rates of stenosis in the left common carotid artery were found in CNPP clean-up workers with ARS (12.0 ±19.2) compared to CNPP evacuees (4.6 ±13.3, $p<0.05$) and veterans (2.0 ±10.4, $p<0.02$). Highest indicators of a stenosis of the left internal carotid artery were found among those diagnosed with ARS (3.2 ±10.4) among all Chernobyl survivors ($p<0.05$).

	brain mapping of the main frequency ranges spectral analysis • Ultrasound scans of cerebral and neck vessels The study examined PTSD and other mental health disorders in Chernobyl Nuclear Power Plant (CNPP) clean-up workers with PTSD (with and without Acute Radiation Sickness [ARS]), and evacuees of Chernobyl exclusion zone with PTSD compared with Afghanistan veterans of war with PTSD and mild closed head injury and a control group of health people not exposed to ionizing radiation.			
Mishcheniuk, O.Y., et al.	Ph-negative Myeloproliferative neoplasms (MPN) patients had demographics (sex and age), history of thrombosis, spleen diameter (by ultrasound), peripheral blood sample (hemoglobin and cell county), and molecular parameters data collected. The study aimed at understanding how the JAK2V617F mutation or coexisting throbophilic risk factors contribute to	Ukraine, 2009-2013, Males & Females	Cross-sectional study of 198 patients. All patients were divided into 3 groups: PV (polychythemia vera), ET (essential thrombocythemia) and PMF (primary myelofibrosis). For each group, patients were divided into exposed and nonexposed to Chernobyl radiation.	PV and ET patients in both exposed and nonexposed subgroups were comparable in terms of the prevalence of the JAK2V617F mutation (96.1% vs. 96.4% and 50% vs. 61.4%, respectively). No significant differences existed in clinical parameters between Chernobyl exposed and nonexposed. In PMF patients the frequency of the G1691A allele of factor V gene was significantly higher in patients with thrombosis than those without thrombotic episodes (p=0.03). The trend continued to those exposed (p=0.05), but was not observed in nonexposed (no carriers, not applicable).

	thrombotic complications in patients with Ph-negative MPN. Ph-negative MPN patients exposed to radiation due to Chernobyl were compared with Ph-negative MPN, nonexposed patients.			Higher prevalence of the G1691A allele of factor V and/or G20210A allele of prothrombin gene was confirmed in exposed patients with thrombosis compared to those exposed without thrombosis (3 of 13 vs. 0 of 32 patients, p=0.02). Prevalence of G1691A allele of factor V and/or G20210A allele of prothrombin gene was not significantly different between those with thrombosis compared to those without thrombosis (3 of 40 versus 3 of 113 patients, p=0.18)
Mykhaylov, V. and Zdesenko, I.	Clinical psychopathological, instrumental and biochemical methods were used to assess the clinical structure and dynamics of non-psychic psychic disorders within psychic-neurological disorders in persons exposed to radiation due to the Chernobyl accident. Patients who were exposed to Chernobyl radiation were evaluated and followed. An intervention that included medication, psychotherapy, and social therapy was developed. The exposed group was compared with a control group in terms of success of the rehabilitation program.	Ukraine, 1986-2013, Males	Prospective study of 300 adult patients, who were 30-45 years old in 1986	Patients were assessed at four stages: Stage #1(1986-1989): patients were identified in 3 groups: group 1 "Vegetative-Vascular"=53%, group 2 Chronic Cerebral Ischemia= 41%, and group 3 Acute Cerebral Circulation Disorders= 6%. Clinical syndromes: asthenia= 86%, neurasthenic syndrome= 14%, liquor hypertension= 37.6%, vestibular syndrome=16.8%, and paroxysmal syndrome= 54%. Stage #2 (1990-1993): no changes were seen. Stage #3 (1994-1999): asthenic syndrome transitioned from physiogenic to psychogenic: Hypochondria=18%, Sub-depression= 17.9%, Obsession =6.9% and Hysteria=17.1%. Patients also presented with: Cognitive Deficiency Syndrome= 38%, Hypertension= 27% and Cerebral Atherosclerosis= 5%. Stage #4 (2000-present): increased "organic" processes with decreased neurotic disorders. Hypertension increased to 47% of patients as well as Cerebral Atherosclerosis to 23% and Cerebral Stroke to 12%.

				Encephalopathy developed in 69% of patients.

Table 6. Literature Review: Findings on Respiratory Disease (2013 review update)

Findings on Respiratory Diseases				
Reference	Source Description	Country, Period, Sex	Size (N), Type, Age (yrs)	Results
Grigoriev, P., et al.	Data from the National Committee of Statistics of Belarus were examined and Age-standardized Death Rates (SDR) were calculated. The study aimed at identifying temporal changes in overall and cause-specific mortality, compare areas contaminated due to Chernobyl with the rest of the country and link mortality to socio-economic indicators across regions.	Belarus, 1997-2007, Males & Females	Cross-sectional study of people in Belarus.	Respiratory diseases not a main cause of death, but had a large influence on inter-regional mortality differences. In two regions, the Vitebsk and Grodno oblast, mortality due to respiratory diseases was much higher than in other oblasts. There was an apparent cluster of high mortality from respiratory diseases in the northern part of the country.
Rahu, K., et al.	Used the Estonian Causes of Death Registry and assessed risk of death from different causes by the Standardized Mortality Ratio (SMR)-expressed as a ratio of observed to expected number of cases. Risk of death (mortality risk) was examined for Estonian Chernobyl Nuclear Power Plant (CNPP) clean-up workers cohort (assembled in 1992 from several data sources) compared to the Estonian male population.	Estonia, 1986-2011, Males	The update of results was conducted on 4,810 adults.	Mortality rates for respiratory diseases were not found to be higher in CNPP clean-up workers compared to the Estonian male population.

Table 7. Summary of Findings from the 2011 Systematic Review

Topics (N= # of studies)	Key Findings – 2011 Review
Anxiety (N=14)	Exposed groups had higher anxiety scores than non-exposed groups. Mothers of exposed children had higher level of concern regarding their child's health and had greater fear for future Chernobyl consequences. Unclear whether increased time since the disaster lessened the anxiety caused by the disaster. Two studies showed that within the exposed groups, the level of anxiety experienced was inversely related to distance from the accident site.
Depression (N=11)	Exposed groups had less favorable scores for depression than non-exposed groups. Unclear whether increasing time since the disaster was associated with decreased depression symptoms. Two studies showed that within the exposed groups, the amount of depression experienced was inversely related to distance from the accident site.
PTSD (N=7)	Exposed groups had higher PTSD scores than non-exposed groups. Evacuated mothers were twice as likely to have health concerns regarding PTSD for their children than non-evacuated mothers. One study showed increasing time since the disaster was associated with lower PTSD scores. Two studies showed that within the exposed groups, the frequency of PTSD experienced was inversely related to distance from the accident site.
Well-Being (N=23)	Exposed groups had higher scores related to poor well-being than non-exposed groups. Unclear whether increased time since the disaster reduced the poor well-being caused by the disaster. Two studies showed that within the exposed groups, the loss of well-being experienced was inversely related to distance from the accident site.
Cognition (N=18)	Exposed groups generally had lower cognitive scores than non-exposed groups, but mixed results were found in children who were irradiated *in utero*. Unclear whether increasing time since the disaster or levels of exposure were associated with poorer cognitive functioning.

Table 8. Summary of Findings from the 2013 Systematic Review

Topics (N= # of studies)	Key Findings – 2013 Review
Reproductive Health (N=14)	Decreased birth rates were found immediately after the disaster in Ukraine, Belarus, Italy, and Sweden. Two studies found birth malformations to significantly increase from before to after the disaster in Belarus. Two studies showed a reduction in number of newborn boys after the disaster in Czech Republic. One study found lower percentage of normal forms of spermatozoa in Chernobyl clean-up workers than control group, but another study found no difference between the clean-up workers and the control group.
Suicide (N=4)	Significantly increased SMR for suicide was found between 1986 and 2002 for a cohort of Chernobyl clean-up workers. Suicidal ideation was more prevalent in clean-up workers than in controls.
CVD (N=8)	Two studies found no increase in SMR for CVD in a cohort of Chernobyl clean-up workers after the disaster. Three studies found higher prevalence of cardiovascular disorders in more-exposed groups than less-exposed groups,
Respiratory Disease (N=2)	One study found higher frequency of respiratory disorders in Chernobyl clean-up workers and exposed children when compared to less-exposed groups. One study showed that airway obstruction and restriction in children increased with higher levels of soil contamination.
Immune Function and Blood Disorders (N=5)	Three studies showed that the activity and number of white blood cells in clean-up workers and exposed children were generally not significantly different to the non-exposed groups, except for few lymphocyte subpopulations. One study found the morbidity rate for blood and blood-forming tissue diseases in Belarus was higher for clean-up workers and evacuees when compared to non-exposed groups.

Table 9. Summary of Findings from the 2014 Systematic Review

Topics (N= # of studies)	Key Findings – 2014 Review
Neuropsychological Consequences (N=3)	Anxiety about radiation exposure is a factor that affects the mental health of the younger generation affected by Chernobyl. Over time, several studies suggested psychological disorders had consequences for non-communicable diseases.
Suicide (N=2)	Death from external causes (including suicide) was the second leading cause of mortality in Belarus. There were findings of continued excess of mortality for suicide in Estonian clean-up workers compared to the general male population in Estonia.
CVD (N=5)	Chernobyl clean-up workers were found to have structural and functional differences in biomarkers thought to relate to disease severity. While not solely attributed to the accident, CVD was found to be the main cause of death in Belarus. Those exposed were found to have reduced endothelial regeneration and repair capacity, possibly placing Chernobyl survivors at a higher risk of developing cardiovascular complications. Over time, there was an increase in prevalence of hypertension in Chernobyl exposed subjects.
Respiratory Disease (N=2)	Mortality due to respiratory disease was different across Belarus, but was not an overall main cause of death. Similarly, in Estonia, clean-up workers did not have significantly higher mortality rates due to respiratory diseases, compared to the general male population.

Table 10. Recommendations from the 2011 &2013 Reports

Recommendations from the 2011 & 2013 Reports
• A systematic assessment of ongoing research and programs related to neuropsychological consequences of the disaster should be carried out. At the least, the survey should cover Ukraine, Belarus, Russia, and Moldova. This assessment could be carried out using the resources of the Green Cross offices within each country.
• Data should be collected that will directly address the need for services and other interventions in the populations that continue to be affected by the Chernobyl disaster. These populations can be defined on a geographic basis. o The literature reviewed in this report, the focus group findings, and the expertise of researchers and practitioners in the affected areas should be the basis for developing a brief instrument that could be readily implemented and that would provide findings useful for guiding program development. o There are a number of institutions with relevant expertise and experience that should be collectively involved in developing the instrument and the general approach. There are also researchers external to Eastern Europe who should be involved, e.g., Dr. Evelyn Bromet. o While ideally, data would be collected through population surveys, more practical and feasible approaches might be used, such as approaching people in clinics, worksites, and educational institutions. o Multi-country studies carried out with standardized instruments and uniform protocols may be particularly informative.
• A major uncertainty, not addressed in this report, is the potential for further data to motivate action, whether by governmental or non-governmental organizations. A "mapping" or a description of the "actors" in each country would be valuable and needed to understand how further data collection on the neuropsychological consequences of the disaster could make a difference.
• Further research, beyond the programmatically-oriented data collection proposed above, could be useful. There have been studies of the long-term neuropsychological consequences of disasters of various types, but the exposures of Chernobyl are unique. Information might be gained that would relevant to the current crisis in Japan.
• We concur with the recommendation made recently by Bromet et al. (Bromet et al. 2011) that the possibility of augmenting ongoing epidemiological studies to address neuropsychological consequences of the disaster should be explored.
• At the 25th anniversary year of the disaster, it would be timely to give greater discussion to the topic of long-term neuropsychological consequences. The planned 25th anniversary conference, for example, “Twenty-five Years after Chernobyl Accident. Safety for the Future”, Kyiv, April 20-22, 2011, does not appear to give any emphasis to this topic. o Funding should be sought for holding a conference with the goals of further characterizing the current state of the evidence, obtaining input into developing a data collection instrument, defining further research needs, and establishing a network of collaborators.
• We recommend further research on non-communicable diseases, such as cardiovascular diseases, only if sufficient resources can be identified to carry out studies that will give meaningful results that will benefit the survivors. o If a decision is made to carry out a new population-based epidemiological study, a sufficiently large population would be needed for cardiovascular diseases; both Chernobyl-affected people and controls would need to be included; and careful and comprehensive assessment of exposures and outcomes would be requisite. Ideally, the study population would come from the four most affected countries.

Recommendations for SOCMED Program

- Extending the successful and integrated components of the SOCMED programming to cover additional regions, supplementing further outreach efforts, and including specialized interventions would be an appropriate long-term strategy.
    - Focusing on reversing stigmatization through education. Reversing stigmatization can be a challenging task, but efforts should be made within the SOCMED projects or within the program as a whole. For example, a large media campaign, including well-known and respected opinion leaders (such as politicians, athletes, and movie stars who belong to affected families), could be a starting point to bring this discussion to the forefront and help change public perception.
    - Reversing adverse lifestyle risk factor profiles should be given consideration. It is known that cardiovascular diseases can be enhanced by direct and indirect factors, such as stress and lifestyle. These are key determinants of risk for cardiovascular diseases. The adults in the affected countries have high prevalence rates of well-known disease risk factors – smoking and excessive alcohol, for example, and obesity is rising. The SOCMED program should embed health promotion and countermeasures in its activities. For example, educating and monitoring blood pressure among the participants, especially those in the family clubs, could help.
    - Depression, anxiety, and suicide remain critical concerns also for focus group participants. Consideration should be given to roles of the SOCMED projects in identifying, educating, and referring affected people to receive appropriate support. For example, creating dialogue about these topics in family clubs and therapy camps could help bring attention to these problems and perhaps allow participants to share their own stories which help them in finding solutions. In addition, strategic partnerships with local institutions should be considered to allow participants or people identified by the SOCMED outreach team to receive help at affordable or no cost.
    - Many additional activities could be proposed to strengthen the SOCMED projects (for example, examining the causes of low-vision among children at the therapy camps, and further examining the blood-related problems in the family clubs). An approach for strengthening activities and giving priorities is needed; a formal evaluation of existing programs may be of benefit in this regard. Conducting a comprehensive program evaluation and needs assessment for the SOCMED program, especially for the medical approach in the projects, will identify opportunities to integrate and strengthen projects further for additional health issues.
    - Strengthen the existing nutrition projects within the SOCMED program, which currently focus in reducing the uptake of radionuclides via food consumption and assuring that any excess radiation dose is minimized. Such interventions could be strengthened in the family clubs and therapy camps. Nutrition projects could also include education on healthy diet and the use of dietary supplements, such as vitamins. For example, the consumption of folic acid has shown to reduce neural tube defects. Nutritional deficiencies could contribute to anemia, found in some studies.
    - In addition, the SOCMED program could be an opportunity to further investigate the long-term health consequences of the Chernobyl disaster. Using routine activities and programming, the SOCMED program might be able to collect and evaluate data from participants in the projects, accumulating a cohort for follow-up. We recommend an evaluation of this opportunity.

Appendix A. Acronyms for Measurements in the Studies

Acronym	Questionnaire	Measure	Reference Given (1st author)
GHQ-12	General Health Questionnaire (12 items)	Minor psychiatric disorders in the general population	Masunaga, T.
BPRS	Brief Psychiatric Rating Scale	Anxiety, Depression	Loganovsky, K.N.
Spilberger-Khainin Anxiety Scale	Spilberger-Khainin Anxiety Scale	Trait and State Anxiety	
IDA	Irritability, Depression, Anxiety Scale	Anxiety, Depression	
SDS	Zung Self-Rating Depression Scale	Depression	
IES	Impact of Events Scale	PTSD	
IES-R	Impact of Events Scale-Revised	PTSD	
Mississippi PTSD Scale	Mississippi PTSD Scale	PTSD	
"Radiation" PTSD questionnaire	"Radiation" PTSD questionnaire	PTSD	
GHQ-28	General Health Questionnaire (28 items)	Minor psychiatric disorders in the general population	
FSS	Functional Systems Score	Well-Being	
EDSS	Expanded Disability Status Scale	Well-Being	
RAVLT	Rey Auditory Verbal Learning Test	Cognition	
SKT	Short Cognitive Performance Test	Cognition	

Appendix B. Additional Studies Published Prior to February 2013

Five additional studies that were published prior to 2013 and were not included in our previous report are summarized here. The studies include an update from Adams, R.E. and colleagues[54] on their previous work related to the long-term mental health of women living in Kiev at the time of the disaster. Another study by Cwikel, J.G. and colleagues[55] reported results from their 1994 data collection period on life events, negative assessment and psychological measure (e.g., PTSD, depression, and anxiety). Belyi, D. and colleagues[56] conducted a study from 1986 to 2008 on 190 adults exposed to Chernobyl and monitored by the Kiev-Research Center for Radiation Medicine (RCRM). A study by Kholodova, N.B. and Zhavoronkova, L.A.[57] conducted examination on 53 Chernobyl clean-up workers in Russia between the years 1990 to 2004. Lastly, a study by Koscheyev, V.S. and colleagues[58] studied long-term effects of the disaster in 94 adults and 50 working adolescents living in the relatively uncontaminated village of Bobrusk in Belarus. The authors administered a questionnaire to understand the participants concerns and worries about radiation and how they felt the government handled dissemination of information about radiation and exposure. Below we present these studies and provide a table highlighting the results.

RESULTS

Neuropsychological Consequences

Adams, R.E. and colleagues[54] studied the long-term mental health consequences for 797 women living in Kyiv at the time of the disaster. The authors contacted women previously recruited in 1997 to complete questionnaires and assess mental health 19 years post the Chernobyl disaster. All women in the study were exposed to factors associated with Chernobyl at different levels, including the population-based control group of the study. The authors used the Impact of Events Scale-Revised (IES-R), the major depression module of the WHO version of the Composite International Diagnostic Interview (CIDI 2.0) and the abbreviated version of the Symptom Checklist-90 to assess psychological well-being of mothers who were pregnant or had small children at the time of the disaster. Due to a skewed distribution, the top 25% and bottom 75% cut-off points were used to evaluate levels of stress[54]. The study found that evacuees reported more risk perceptions than the neighborhood controls (X^2=77.20, p<0.001) and the population-based controls (X^2=114.20, p<0.001). No significant difference was found for Chernobyl-related coping behaviors between evacuees and the neighborhood controls (X^2=0.80) and evacuees and population-based controls (X^2=0.03). Adams, R.E. and colleagues[54] also found a difference in Chernobyl-related PTSD, Major Depressive Episodes (MDE), and high stress between evacuees and neighborhood controls (X^2=15.30, p<0.001; X^2=7.14, p<0.01; X^2=13.64, p<0.001, respectively) and difference in Chernobyl-related PTSD and high stress between evacuees and population-based controls (X^2=19.08, p<0.001; X^2=11.53, p<0.001, respectively). Adjusting for all risk factors including risk perceptions, group status (being an evacuee vs. neighborhood control or population-based control) was not a predictor of any of the mental health outcomes. Lastly, the study found that compared to women reporting low risk perceptions, women reporting high Chernobyl risk perceptions were 8.86 times more likely (95% CI 3.49-22.53, p<0.001) to meet criteria for probable

PTSD, 2.01 times more likely (95% CI 1.18-3.42, p<0.01) to meet criteria for Major Depressive Episodes, and 6.01 times more likely (95% CI 3.15-11.65, p<0.001) to meet high levels of distress[54].

Another study by Cwikel, J.G. and colleagues[55] examined long-term psychological distress (e.g., PTSD) in Chernobyl survivors who immigrated to Israel. The study groups included persons who immigrated from high contamination zones, low contamination zones and other, non-exposed areas. A total of 708 subjects were included, 334 controls and 374 immigrants from areas with different levels of contamination. While the study population was the same as that reported in the article included in our previous review, the focus of this report was on life events and negative assessment from participants about Chernobyl. The authors developed a questionnaire for the study based on 20 open-ended interviews. The questionnaire was developed to measure the subjective evaluation of the Chernobyl accident in subjects and included questions about depression (CES-D depression scale), stress (subscales from the Revised Symptom Checklist- SCL-90-R), stressful life events, and PTSD (15-item Impact of Event Scale- IES). The study found that exposed groups had significantly greater mean scores in all psychological outcome measures compared to the control group[55]. Interestingly, the authors found that the level of PTSD symptoms among the most exposed with no reported recent life events was similar to that of the control group who reported 5 or more recent life events.

Kholodova, N.B. and Zhavoronkova, L.A.[57] conducted a study to understand the nervous system pathology of Chernobyl clean-up workers. The authors performed neurological investigations, electroencephalography tests and used a programmable MBN-Neirokartograf instrument to assess EEG coherence. Fifty-three clean-up workers, ages 24-41 at start of the study were followed from 1990-2004. Tests were performed at three follow-up intervals 1990-1992, 1993-1998, and 1999-2004. During 3 separate follow-up periods, the clinical examinations and EEGs showed what the authors described as signs of brain aging[57]. The study found a decrease in memory and slowing of mental processes over time with 14% of participants showing a normal EEG at the start of the study, but none at both follow-up times. A flat EEG was evident in 17% of participants at start of the study and increased to 37% and 51% of participants at the 1993-1998 and 1999-2004 follow-up periods, respectively. At the start of the study, 24% of participants presented with an EEG showing hypersynchronous with accelerated alpha rhythm, by the first follow-up the percent had reduced to 20 and by the second follow-up this type of EEG was evident in 5% of participants. The study did not conduct any statistical analysis and the methods were not described in detail. The authors reported a mean number of illnesses per patient that increased from 5.8 in 1990-1991 to 12.4 in 2004[55]. Kholodova, N.B. and Zhavoronkova, L.A. also reported negative changes (decreases in biopotentials) in all participants. By the end of the end of the study, 51% of participants showed a flat EEG, 44% showed a hypersynchronous with slowed alpha rhythm, and 5% showed an EEG with hypersynchronous with accelerated alpha rhythm.

Another study by Koscheyev, V.S. and colleagues[58] studied the long-term psychosocial effects of the Chernobyl accident in adults and adolescents living in the Belarusian village of Bobrusk, which is considered to be relatively uncontaminated. A total of 144 participants completed the Russian Language Radiation Concerns Questionnaire, a survey created for this investigation. The authors reported internal consistency of the psychometric properties for the adult survey at Cronbach's alpha=0.77 and an alpha reliability of 0.44 for the adolescent version. The study showed that both adults and adolescents (even

adolescents that don't remember the Chernobyl accident well) continue to have health concerns for them and family members related to the accident. Almost half of the adult participants, 48.9%, and 38% of adolescents reported thinking about Chernobyl. Participants were asked about feeling aches and pain themselves or those experienced by their family members and worrying that these were problems caused by radiation exposure. A large proportion of adults, 55.3%, and 28% of adolescents worry that the aches and pain were caused by radiation, while 64.9% of adults and 36% of adolescents confirmed a worry about the aches and pain their family members experienced. The study also found a high distrust of government information about the health effects of Chernobyl, with 92.4% of adults and 74% of adolescents answering that they did not feel or were unsure that the government gave accurate information about the disaster.

Immune Function and Other Blood-related Disorders

Among different non-cancer effects of acute radiation, Belyi, D. and colleagues[56] studied the effects of radiation on hematology. The descriptive study included patients diagnosed with ARS (n=91)—with mild, moderate and severe ARS—and a control group of 99 patients who were exposed at levels below 1.0 Gy. Follow-up activities were conducted in 1986-1991, 1992-1996, 1997-2001, and 2002-2008, where all patients were examined at least one time during each period. The study found that both ARS patients and controls presented with transient residual cytopenia, although it was at a higher frequency for ARS patients. During the 1986-1991 follow-up period, frequency of cytopenia was higher compared to the 2002-2008 period, and all types of cytopenia were statistically higher in ARS patients compared to controls in 1986-1991: 1) Granulocytopenia: ARS= 40.7% vs. controls=26.9% ($p<0.05$), 2) Lymphocytopenia: ARS=72.5% vs. controls=40.9% ($p<0.001$), 3) Thrombocytopenia: ARS=58.2% vs. controls= 23.7% ($p<0.001$), and 4) Erythrocytopenia: ARS=60.4% vs. controls 37.6% ($p<0.001$). This was not the case in the 2002-2008 follow-up period, which the authors concluded the ARS group restored this function.

Cardiovascular Disease

Belyi, D. and colleagues[56] also studied CVD. They reported 74 ARS patients and 79 controls developing arterial hypertension, and 22 ARS patients and 27 controls developing coronary heart disease during the follow-up period. The authors did not find a significant different between ARS patients and controls with regards to selected CVD risk factors. The study design limited the authors from estimating the role of CVD risk factors and accurately estimating dosimetric doses[56].

Table 11. Literature Review: Additional Findings on Neuropsychological and Non-cancer Outcomes Prior to February 2013

Additional Findings of Articles Published Prior to February 2013				
Reference	Source Description	Country, Period, Sex	Size (N), Type, Age (yrs)	Results
Adams, R. E., et al. (2011)	Studied the long-term mental health consequences 19 years after Chernobyl of women living in Kyiv at the time of the disaster who were pregnant or had small children. Scales used to assess psychological well-being: • Impact of Events Scale-Revised(IES-R) • The major depression module of the WHO version of the Composite International Diagnostic Interview (CIDI 3.0) • Symptom Checklis-90 (abbreviated version) • Life stress was measured by: 1) lack of basic necessities, 2)lack of adequate skills to live in Ukraine's socioeconomic conditions	Ukraine, 2005-2006, Females	Cross-sectional study of 797 women who were originally recruited for a study in 1997 (Bromet et al., 2000): Groups: 1) Evacuees (E) n= 254 2) Neighborhood controls (N Controls)= 239 3) Population-based controls (P Controls)= 304	No significant difference between the three groups for Chernobyl-related coping behaviors. Comparison between evacuees and neighborhood controls: • High Chernobyl risk perceptions (4-6 perceptions endorsed): o E= 48% o N Controls= 16.7% o P Controls= 10.9% o E vs. N controls: X^2= 77.20 (p<0.001) o E vs. P controls: X^2= 114.20 (p<0.001) • Chernobyl-related PTSD: o E= 19.7% o N Controls= 7.5% o P Controls= 7.2% o E vs. N controls: X^2= 15.30 (p<0.001) o E vs. P controls: X^2= 19.08 (p<0.001) • Major Depression episodes (past year): o E= 29.1% o N Controls= 18.8% o P Controls= 29.9% o E vs. N controls: X^2= 7.14 (p<0.01) o E vs. P controls: X^2= 0.04 (not statistically significant) • High Stress: o E= 26.8% o N Controls= 13.4% o P Controls= 15.1% o E vs. N controls: X^2= 13.64 (p<0.001) o E vs. P controls: X^2= 11.53 (p<0.001)
Belyi, D., et al.	To understand long-term non-cancer effects of ionizing	Ukraine, 1986-2008	Descriptive study of 190 adults with exposure	Hematopoietic changes 1986-1991: • Granulocytopenia less than

(2010)	radiation patients at the Kiev-Research Center for Radiation Medicine (RCRM) who were diagnosed with Acute Radiation Syndrome (ARS) compared to patients who were exposed to lower doses, not exceeding 1.0 Gy.		from Chernobyl accident. Groups: 1) ARS n=91 (mild, moderate and severe ARS) 2) patients with doses of exposure not exceeding 1.0 Gy n=99	2,000 μL^{-1} o ARS= 40.7% vs Controls= 26.9% ($p<0.05$) • Lymphocytopenia less than 1,200 μL^{-1} o ARS= 72.5% vs Controls= 40.9% ($p<0.001$) • Thrombocytopenia less than 150 x 10^3 μL^{-1} o ARS= 58.2% vs Controls= 23.7% ($p<0.001$) • Erythrocytopenia (for men less than 4.3 x 10^{-6} μL^{-1}; for women less than 3.8 x 10^{-6} μL^{-1}) o ARS= 60.4% vs Controls= 37.6% ($p<0.01$) 2002-2008 follow-up: • Granulocytopenia less than 2,000 μL^{-1} o ARS= 3.2% vs Controls= 4.8% (not statistically significant) • Lymphocytopenia less than 1,200 μL^{-1} o ARS= 9.7% vs Controls= 19.4% (not statistically significant) • Thrombocytopenia less than 150 x 10^3 μL^{-1} o ARS= 8.1% vs Controls= 6.5% (not statistically significant) • Erythrocytopenia (for men less than 4.3 x 10^{-6} μL^{-1}; for women less than 3.8 x 10^{-6} μL^{-1}) o ARS= 45.2% vs Controls= 37.1% (not statistically significant) CVD 1986-2008: • Development of arterial hypertension (AH): o ARS= 74 patients o Controls= 79 patients • Coronary heart disease (CHD):

				o ARS= 22 patients o Controls= 27 patients Morbidity rates due to non-cancer diseases were not statistically different between ARS and control groups.
Cwikel, J.G., et al. (2000)	To examine the long-term psychological distress of Chernobyl survivors (from high contamination and low contamination zones) who immigrated to Israel compared to immigrants from other countries. Scales used to assess psychological well-being: • Impact of Event (IES) for PTSD • Subscales from the Revised Symptom Checklist (SCL-90-R) for stress • CES-D depression scale for depression	Israel, 1994, Males & Females.	Cross-sectional study of 708 immigrants, ages 16 and older. Groups: 1) Chernobyl high contamination zone n=137 2)Chernobyl low contamination zone n=240 3) Immigrants from other countries (not exposed) n=331	Life Events • 86.4% of subjects reported at least one major life event since 1986 (range 1-10 events; mean= 3.2±2.2) • Life events reported: o Financial problems = 51% o Housing, work, unemployment, illness= about 1/3 of sample o Death of a relative= 1/3 of the sample o Death of a spouse= 5% o Marital problems= statistical difference found between groups X^2= 6.3, p= 0.04 o Illness of self/family member= statistical difference found between the groups X^2= 9.3, p= 0.009 Psychological Outcomes by number of life events and exposure (adjusting for covariates) • PTSD: o # of life events: β= 0.25 (p<0.001) o Exposure: β= 0.34 (p<0.001) • Depression: o # of life events: β= 0.21 (p<0.001) o Exposure: β= 0.12 (p<0.01) • Anxiety: o # of life events: β= 0.21 (p<0.001)

				○ Exposure: β= 0.13 (p<0.001) ○ Psychological Outcomes by negative assessment of events, not controlling for exposure and controlling for exposure (adjusting for covariates) • PTSD (effect of negative assessment does not retain its main effect after controlling for exposure, effect decreases by about 30%): ○ Not controlling for exposure: β= 0.38 (p<0.001) ○ Controlling for exposure: β= 0.26 (p<0.001) • Depression (effect of negative assessment retains its main effect after controlling for exposure): ○ Not controlling for exposure: β= 0.24 (p<0.001) ○ Controlling for exposure: β= 0.25 (p<0.001) • Anxiety (effect of negative assessment retains its main effect after controlling for exposure): ○ Not controlling for exposure: β= 0.20 (p<0.001) ○ Controlling for exposure: β= 0.18 (p<0.01)
Kholodova, N.B. and Zhavoronkova, L.A. (2011)	Understand the nervous system pathology of Chernobyl clean-up workers over a period of 14 years using electroencephalography and neurological investigations.	Russia, 1990-2004	Prospective study of 53 Chernobyl clean-up workers.	1990-1992: • 11 patients considered invalids • 14 had normal EEG • 17 had flat EEG • 45 had hypersynchronous with slowed α rhythm EEG • 24 had hypersynchronous with accelerated α rhythm EEG 1993-1998: • 26 patients considered invalids

				• 0 had normal EEG • 37 had flat EEG • 43 had hypersynchronous with slowed α rhythm EEG • 20 had hypersynchronous with accelerated α rhythm EEG 1999-2004: • 53 patients considered invalids • 0 had normal EEG • 51 had flat EEG • 44 had hypersynchronous with slowed α rhythm EEG • 5 had hypersynchronous with accelerated α rhythm EEG Mean number of illnesses per patient increased from 5.8 in the first investigation in 1990 to 12.4 in 2004.
Koscheyev, V.S., et al. (1997)	To examine the long-term effects of the disaster in adults and adolescents living in Bobrusk, a village in Belarus considered being relatively uncontaminated. The questionnaire used was the Russian Language Radiation Concerns Questionnaire (adults= 31 items, adolescent= 26 items).	Belarus	Cross-sectional study of 94 adults and 50 working adolescents in the Belarussian village of Bobrusk.	Selected endorsement of radiation concerns • Length of time subject thought about the accident every day: o Adults: still think about it every day or almost every day= 35.1% o Adolescents: still think about it every day or almost every day= 16%, don't remember the accident= 50% • Thinking about the accident in the past 3 months (every day to every 2-4 weeks): o Adults= 48.9% o Adolescents= 38% • "Don't Know" response for how much radiation they had been exposed to after the accident: o Adults= 44.7% o Adolescents= 60% • Worry about aches and pains being caused by the radiation (yes): o Adults= 55.3% o Adolescents= 28%

				• Worry about family members' aches and pains being caused by the radiation (yes): o Adults= 64.9% o Adolescents= 36% • In the year after Chernobyl, government gave accurate information about health effects of the disaster (no/unsure): o Adults= 92.4% o Adolescents= 74%

Appendix C: Additional Studies from Non-English Literature and Grey Literature Search

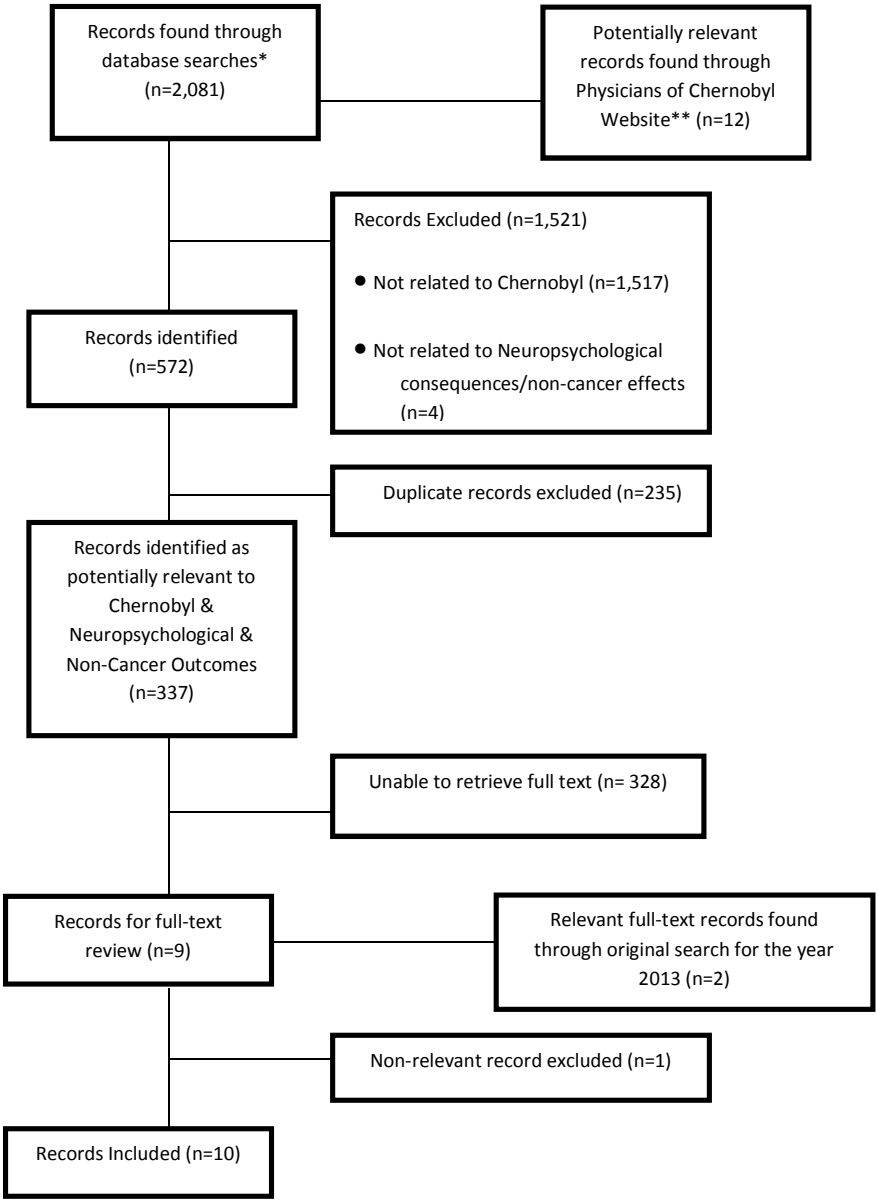
In addition to our original searches involving peer-reviewed studies (see Table 1 for search words), we conducted additional searches to access local "grey" literature and non-English literature. The term "grey literature" refers to documents from different industries that are not published in peer-reviewed journals, and can include reports (e.g., government or private industry reports) and non-published articles. The search for grey literature involved using the Google search engine to find reports or information on Chernobyl by using the search phrases "Chernobyl AND non-cancer effects" and "Chernobyl AND neuropsychological consequences". The search returned reports already included in our previous literature reviews (Samet & Patel 2011 & 2013) from organizations such as the WHO, the European Committee on Radiation Risk (ECRR), the International Atomic Energy Agency (IAEA), and the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). Our colleagues provided us with a list of names of possible researchers in the field. We searched names of local physicians and scientists involved in research pertaining to the Chernobyl disaster that could provide us with information on relevant studies and reports. Attempts were made to contact local researchers via email; however these were all unsuccessful.

The searches for grey literature and researchers led us to find an organization named Physicians of Chernobyl (website: www.physiciansofchernobyl.org)[59]. Led by Dr. Angelina I. Nyagu (president), the association has collaborated with NGOs to organize conferences where scientists and physicians discuss the effects of the Chernobyl accident and the impact on multiple populations. Disseminating information about the aftermath of the disaster and publishing a journal are major goals of the organization. The journal published by the Association Physicians of Chernobyl is titled *International Journal of Radiation Medicine* (online access for years 1999 to 2006). While the journal did not appear in PubMed, online access through the association's website included free access to PDF files of the articles published in the years 1999-2006. Each issue of the *International Journal of Radiation Medicine* was reviewed and potentially relevant articles were extracted for full-text review. Between 1999 and 2006, the *International Journal of Radiation Medicine* published 8 articles pertaining to neuropsychological and non-cancer effects of the Chernobyl disaster that met the criteria for this review. The articles focused on mental and general well-being, PTSD, anxiety and depression, suicide, CVD, immune and other blood related disorders, and reproductive health.

We also used PubMed to conduct a second review on the original search terms found in Table 1 and extract all non-English literature. Additionally, the names of reserachers provided by colleagues and those found online via Google were also searched to examine any articles appearing in PubMed. Our team also compiled a list of foreign journals that appeared multiple times and a search in PubMed (in conjunction with the word "Chernobyl") was conducted to locate additional articles that may have been missed in the previous searches. Initial review included checking the title and abstract, when available, for potential relevance to the focus of this review. In total, 2,081 articles in languages other than English (primarily Russian) were found. Of these, 1,521 were excluded as being out of the scope of this report. After removing non-relevant publications and duplicates, three hundred and twenty-nine (329)

potentially relevant, non-English articles were retrieved via PubMed using author, journal and original search strategies. During this review, our team had full-text access to only 1 of 329 publications. Tables 19 to 27 list the 328 references found that we did not have full-text access by topic. The the results summarized below pertain to the findings from the 8 non-English articles published in the *International Journal of Radiation Medicine* and the additional 2 articles published in 2013 found in the original search queries. The 2 articles were translated using Google Translate and the English abstracts provided by the authors were used to ensure appropriate translation and interpretation of the results. A total of 10 non-English articles are included in this update to the literature. Tables 12-16 highlight findings from each of the non-English articles by topic in order of publication date. A number of these article use unconventional terminology from the point of view of conventional medicine in the United States and Europe. We have retained the authors' original terms and offer definitions when possible. A separate PRISMA diagram for the non-English and grey literature study selection was prepared and appears below.

Figure 2: PRISMA Diagram for Study Selection: Non-English and Grey Literature



RESULTS

Neuropsychological Consequences and Suicide

Nyagu, A.I. and colleagues[60] published a study in 1999 examining the psychological consequences of the Chernobyl disaster. The study conducted included 200 patients divided into 6 groups: 1) 70 men diagnosed with ARS, 2) 80 men who were liquidators after the Chernobyl accident—subdivided into group A) those who were at the site for less than 3 months [n=37] and group B) those

who were at the site for 3+ years [n=43], 3) 15 healthy persons, 4) 15 patients with "dyscirculatory encephalopathy", and 5) 20 veterans of the Afghanistan war with PTSD. The term dyscirculatory encephalopathy is commonly used in Russian and Ukrainean medicine. While our team could not find a specific definition, studies published give an understanding of the disease. Hence, we rely on the authors' descriptions and terminology. Alone, the term encephalopathy alludes to brain disease or damage that has different causes and manifests as an altered mental state. In the case of dyscirculatory encephalopathy, the altered mental state is caused by a dysfuntion in cerebrovascular system. For this study, multiple psychological scales as well as electroencephalography (EEG—conventional and quantitative) and visual evoked potential (VEP) tests were conducted on the patients. Liquidators showed high prevalence of symptoms including headaches (86% of liquidators), memory deterioration (76%), and limb pain (69%)[60]. Depressive mood and irritability were found in 32% and 44% of liquidators. Neuropsychological disorders that were predominantly seen among the liquidators were "sensoric-algetic" disorders (85% of liquidators)–the term "sensoric-algetic" is non-conventional in Western medicine and a search for the definition of the words suggests a sensation of and sensitivity to pain— and autonomic disorders (90%). For both ARS patients and liquidators, the authors report a quick progression (2-5 years) from autonomic-vascular dysfunction to encephalopathy. Liquidators were also found to display emotional withdrawal (BPRS index mean 2.2±0.2 vs. 0.5±0.1 for healthy control group, $p<0.05$), lack of interest with the environment, autism, depressive mood (BPRS index mean 3.6±0.2 vs. 1.2±0.2 for healthy control group, $p<0.01$), and anxiety (BPRS index mean 3.0±0.2 vs. 1.1±0.1 for healthy control group, $p<0.05$) and feelings of despair. Additionally, they presented with spontaneous pain and paresthesia, which the authors note were difficult for them to describe and caused much distress[60]. Negative symptoms were also examined using the Scale for the Assessment of Negative Symptoms (SANS), and findings revealed that liquidators had significantly higher levels of negative symptoms that presented as physical "anergia" or lack of energy, reduction of recreational and sexual interest and activities, social withdrawal, unchanging facial expressions and poor eye contact, among other symptoms. The mean scale index for "affective flattening" (i.e., lack of emotional expression) was calculated at 2.1±0.2 for liquidators compared to 0 for the healthy control group ($p<0.01$). "Anhedonia", or the inability to experience pleasure, had the highest index difference, calculated at 2.6±0.2 for liquidators compared to 0 for healthy controls ($p<0.01$), while "alogia", or the lack of speech, had lowest difference between the two groups (1.9±0.2 vs. 0), albeit still significant at $p<0.01$.

When examining PTSD, Nyagu, A.I. and colleagues[60] found that liquidators scored an average of 34.6±6.7 on the Impact of Event Scale (IES) compared to 28.4±5.6 for those with ARS and 27% of liquidators expressed memories of the disaster that was associated with PTSD. Level of depression, as studied using the Unmasking Depression Self-rating Depression Scale (SDS), was seen on 77% of liquidators (56% had minimal to mild and moderate to marked depression, while 21% had severe to extreme depression). The authors also reported patients in the ARS and liquidator groups having worse self-rating of mental and physical health, as well as having the MMPI-profiles significantly different from other groups[60]. EEG patterns for persons irradiated were different from those of patients not exposed to radiation. In particular, 69% of liquidators displayed a flat polymorphous EEG pattern—a pattern only seen at a higher prevalence in the ARS group. The total spectral power of the EEG showed liquidators having the second highest total spectral delta power, while beta power was highest among liquidators

compared to other groups. Both theta and alpha spectral power was lowest among ARS patients followed by liquidators. In addition to the tests performed, Nyagu, A.I. and colleagues[60] analyzed the data comparing liquidators based on time of length at Chernobyl site and dose received. Their findings revealed that doses higher than 0.3 Gy increased delta power and decreased alpha power ($p<0.001$), while duration at the site did not influence changes in spectral power. Among those with doses lower than 0.3 Gy, delta power was significantly different for those with less time at site compared with those who were there for 3-5+ years ($p<0.05$). Among those with doses higher than 0.3Gy, beta power was significantly different between those at the site for a short-term than those who were there for a long-term stay ($p<0.05$).

Frolova, N.S. and colleagues[61] examined 105 Chernobyl disaster liquidators who were 20-50 years old at the time of the accident. The prospective study took place 12-14 years after the disaster. The investigators compared the liquidators to 48 healthy male controls. By the first examination, 65.7% of patients presented with asthenic syndrome (i.e., asthenia, sleep and vegetative nervous system disturbances) and 67.6% of cases presented somatic pathology including arterial hypertensive disease, and ischemic heart disease among others. The majority of liquidators presented with chronic "dyscirculatory encephalopathy" (72.3%), and 64.7% showed signed of disseminated organic neurological symptomatology[61]. Per the authors, "Root reflectory symptoms of spine osteochondrosis" were evident in over half of the liquidators (67.6%), while cerebral cyst adhesive archnoiditis was registered in a smaller percent of liquidators (18%).

Tabachnikov, S.I. and colleagues[62] conducted examinations for 152 liquidators living in Kiev—110 men and 42 women with radiation exposure between 5 and 25 rem—who did not have health problems prior to the Chernobyl accident--but at the time of the study had depressive disorders of a non-psychotic nature. All patients presented with syndromes of depression that included astheno-depressive, depressive-hypochondriac, depressive-phobic, and anxiety-depressive characteristics. Coupled with depression, patients also presented with somatic pathology that included idiopathic hypertension (49.3% of patients), ischemic heart disease (36.2% of patients), dystonia (21.7% of patients), "dyscirculatory encephalopathia" (59.9% of patients), and cerebral arteriosclerosis (28.9% of patients) among other diseases. High anxiety levels were found in 82.2% of patients. In addition to psychological tests, Tabachnikov, S.I. and colleagues[62] conducted electrophysiological and biochemical investigations on patients. Their findings indicated moderately expressed changes in bioelectric activity of the brain and imbalance in chemical levels (e.g., per the authors' description: decreasing levels of noradrenalin and "dofaminum" (dopamine), increasing levels of serotonin in the blood, imbalance of lipid oxidation and endogenous intoxication) of the liquidators of the Chernobyl disaster.

Khomazjuk, I.N. and Goncharenko, L.I.[63] examined 600 participants (1986-1987 LCAS participants with hypertension) with an average external irradiation dose of 218±22 mSv for psychological status and overall quality of life. The control group consisted of 30 participants of LCAS without blood circulation system diseases. Questionnaires, psychological scales and instrumental examination were utilized to understand the psychological and physical health. Findings showed that for 17% of the sample, memories from the Chernobyl accident remained part of the victims' lives; while 9% presented with higher expression of these memories (e.g., problems with dreams). A low percentage of individuals felt

they "were not able to deal with negative senses" of the disaster[63]. A measure of how well individuals deal with the memories from the event is the result from the psychological tests (provided by the authors in the form of an "integral mark"). Results not exceeding an integral mark of 10 were considered satisfactory. Participants who were evacuated from Pripyat showed more negative memories of the disaster than trained employees from the power plant (integral mark 27.9±3.1 vs. 11.1±1.5, $p<0.01$, respectively). The investigators reported negative memories decreasing with time, where they found a 12.6% decrease in the number of people examined during the last 5 years [63]. Compared to the liquidators with hypertension, the control group (those without hypertension) had an average integral mark that was 11 marks lower than that of liquidators (average integral mark of control group= 9±1.1, $p<0.05$). Participants with hypertension presented with higher average integral marks for scales of hypochondria, depression, and hysteria than controls (69.6±2.1 vs. 63.3±1.4, $p<0.05$; 62.7±1.8 vs. 61±2.5 $p>0.05$; 71.2±1.8 vs. 54±2.4, $p<0.01$, respectively). Results for depression were not significantly different between the two groups. The investigators classified participants based on 4 personality types (hysterical, depressive, hypochondriac, and psychoasthenic), those of mixed type (more than one personality type), and those unidentified. Moderate hypertension was seen in all 6 categories, hypochondriac and mixed-type personality types having the highest percentage (93.7% and 92.7%, respectively).

Well-being

Ipatov, A.V. and colleagues[64] published a study in 2004 with the aim of understanding the impact of the Chernobyl accident in the health deterioration of children in Ukrainian provinces. The investigators extracted information from statistic reports to understand the level and prevalence of disability in 6 provinces (Volyn, Zhytomir, Kiev, Rovno, Cherkassy, and Chernygov). The authors found diseases of the nervous system to be the most prevalent with a total of 39.8 cases per 10,000 children in the population in Ukraine. Among the different provinces, diseases of the blood and hemopoietic organs ranged from 1.6-2.6 per 10,000 children in the population. Respiratory diseases ranged from 3.0-11.1 per 10,000 children, while mental and behavioral disorders were much more prevalent at 16.9-37.1 per 10,000 children. Findings show a high level of disability (205.1-237.6 per 10,000 children) among children ages 14-15 years old, which are those born in 1986 and 1987 (irradiated in utero).

Khomazjuk, I.N. and Goncharenko, L.I.[63] quantified quality of life for the participants, and found differences in prevalence for decreasing quality of life between those with hypertension duration up to 5 years compared to those with hypertension for 5-10 years. The highest difference between the groups was a decreasing quality of life due to necessity to receive medical treatment (25% for those with hypertension ≤5 years compared to 75%for those with hypertension 5-10 years).

Yakovlev, P.A. and colleagues[65] published an article in 2005 including 265 children born to liquidators of the Chernobyl disaster who were under medical evaluation. Children were divided into four (4) different age groups born in: 1) 1998-2001 (2-5 year olds), 2) 1993-1997 (6-10 year olds), 3) 1989-1992 (11-14 year olds), and 4) 1988-1989 (15-16 year olds). All children were from the Oryol region. The control group consisted of 131,800 children from the general population living in the "clean" areas of the Oryol region, and whose parents were not liquidators of the Chernobyl disaster. The study

utilized medical examinations and medical records for the children to understand overall well-being and sickness rate of the children exposed to the fallout from the Chernobyl accident. The authors reported sickness rates as "pro mil", and in the accompany figure the rate was denoted by the per mille symbol (o/oo). Based on this information, in this review we report the results as sickness rates per thousand. The investigators found that the sickness rate for those who were children of liquidators was 1.4 times higher than those in the general population, and disease incidence was 1.2 times higher (2,626.4 vs. 1,860.9 per thousand; and 1,470.1 vs. 1,237.7 per thousand, respectively). The authors found a trend in sickness rate, where children of liquidators had higher sickness rates that increased with time. In 1991 the sickness rate for children of liquidators was estimated at 862.5 children per thousand, and in the year 2000 the rate was 1,607.4 children per thousand. For children who lived in contaminated areas, but who were not born to parent liquidators, the sickness rate did not advance as quickly; the authors cite estimates of 473.6 children per thousand in 1991 and in 2003 increasing to 861.8 children per thousand[65]. According to the authors, those who were not born to father-liquidators and reside in "clean" areas had a sickness rate that was fairly constant; in 1991 the estimate was 1,128.7 per thousand and only increased to 1,407.1 per thousand by 2003. Yakovlev, P.A. and colleagues[65] found differences in the number of diseases children were diagnosed with by level of irradiation of the parent. Children who were older (11-14years old) with parents irradiated with more than 25 p (authors' reported measurement units) had the highest average number of diseases diagnosed (3.1 diseases), followed by children whose parents were irradiated at a level of 20-25 p (2.2 diseases). Within the 20-25 p level of parent irradiation, 15-16 years old had a mean of 3.3 diseases. The children of parents irradiated at a level of 10-20 p had a mean of 2.2 diseases.

Korytskyy G. I.[66] conducted a retrospective study to understand the state of health of children in the Ternopil region in Ukraine who were affected by the Chernobyl disaster. This article is one of the two translated using Google Translate. The study focused on children's health indicators in the low contamination area of Ternopil region, and reported access to hospital records (annual medical examination data) for children affected by the Chernobyl disaster (classified as a "victim" of the Chernobyl disaster). Findings suggest a decrease in number of children who are victims of the Chernobyl disaster over time; however, the author states this decrease over the years is due to a change in classification from child and adolescent to adult status (8,994 children in 2003 compared to 7,222 in 2011). The records included information on physical examinations as well as treatment and rehabilitation for the children (e.g., in-patient care, out-patient care, sanatoria and health resorts). A trend reported by the author was a tendency of improvement for the number of children in the areas of Chertkovsky and Ternopil city (number of healthy children ranged from 11-19% during the study period). The author reports the number of children classified as victims as 9,590 in the region; however, in the tables and later text, the author uses n=8,994 for the start year of 2003. It is unclear if the first estimate refers to a previous count of the population. Korytskyy, G.I.[66] conducted a comparison analysis between children classified as "victims" and their peers who were not affected by the Chernobyl accident. The author reports a 1.8-2.5 increase in morbidity for victims of the disaster compared to non-affected peers. A trend of annual growth was indicated[66]. Inconsistency between text and table labels made it impossible for us to accurately understand morbidity in children due to musculoskeletal diseases and digestive diseases when comparisons were made between victims and children no affected by the

disaster. However, the author reported respiratory diseases as the top reason for morbidity in all children in the region. Our team reached out to the author via email to clarify questions, but attempts were unsuccessful.

Kharkovenko R. V.[67] conducted a descriptive study published in 2013 to understand the main diseases affecting victims of the Chernobyl disaster in the Vinnitsa region, Ukraine. The author used data from patient medical records at hospitals and the State Register of Ukraine (2003-2012) to understand causes of morbidity among those affected by the accident. Findings from the study indicate that the health status of liquidators, evacuees, residents of contaminated areas and affected children worsened through the years and fewer individuals from these groups were deemed healthy according to medical examinations. For the group of liquidators, the author reports a decrease of 7.5% to 0.4% in the proportion of individuals with healthy health status from 2003 to 2012 ($p<0.01$). This was also true for evacuees, although the change was about 6 times lower. The investigator reports cardiovascular disease as the top cause of morbidity in the cohort up to 2011, with nearly half (45%) of cardiovascular disease morbidity due to hypertension. Second and third causes of morbidity were due to respiratory and digestive diseases, respectively. In 2012, respiratory diseases became the primary cause of morbidity (33%) and circulatory disease was recorded as 10.5%. Among adult victims, the main cause of all death was circulatory system diseases (77.3%)[67]. Our team translated the article using Google Translate, and the detailed abstract provided by the author in English was used to ensure figures and interpretations were translated appropriately. Two tables in the document, one summarizing total incidence of disease over time for victims and the region, and another reporting the overall mortality for the two groups over time were not used to extract information. For the table on total incidence, it was not clear how the numbers were computed since the label of the table indicated a “per 10,000 population” rate, but the number provided was well above 10,000 (e.g., the author reported total incidence in 2003 for victims as 21,281.4 per 10,000). In the text, the author provided percentages for different causes of morbidity and mortality among the groups; however, the tables seem to combine all diseases, giving an overall number per year. In this report, we have communicated the author’s findings as reported in the text when text and table information were not reported similarly.

Suicide

Tabachnikov, S.I. and colleagues[62] examined suicidal ideology in the group of 152 liquidators. Suicidal ideation was high in this group, with 141 patients (92.8%) having suicidal thoughts. The authors made a distinction between suicidal ideas, statements, intention, action, and uncommitted suicide. Intention, action and uncommitted suicide were highest among those between the ages of 40-49 years old, while suicide ideas was highest among those 50-59 years old (51 patients exhibiting suicide ideas were in this age group). Overall, highest prevalence of suicidal behavior (i.e., intention, action and uncommitted suicides) was seen in those between ages 40-49 years.

Cardiovascular Disease

Khomazjuk, I.N. and Goncharenko, L.I.[63] also evaluated indicators of CVD. Measurements taken from the 600 participants included the thickness of interventricular wall in diastole, thickness of aortic

ventricle back wall in diastole, “power of threshold load at veloergometry”, average daily systolic arterial pressure, average daily diastolic arterial pressure, systolic arterial pressure time index (SAP TI), and daily diastolic arterial pressure time index (DAP TI). The investigators conducted multiple clinical tests including “veloergometry”. The term “veloergometry” is non-conventional and appears in Russian and Bulgarian literature. A search of the term indicates it is a cardiac stress test. Both SAP TI and DAP TI were highest among those with mixed personality types and lowest among depressive type. Statistical significance was not reached when comparisons were made for the different personality types for thickness of interventricular wall to diastole, thickness of aortic ventricle back wall to diastole, and threshold load.

Kostenko, T.A.[68] examined the influence of radiation on the cardiovascular system of children and adolescents in Zhytomir area at 3 timeframes: 1) eight (8), 2) nine (9), and 3) ten to eleven (10-11) years after the accident. The children were relocated from the contaminated area of Zhytomir between 1990 and 1991. The investigator performed clinical observations including exams of the cardiovascular system (e.g., electrocardiographs-ECG, rheoencephalograms-REG, and echocardioscopy-Echo-CS). By 10-11 years post-accident, more than 50% of the children examined showed symptoms of automation functional disorder, sinus arrhythmia, bradycardia and single cases of tachycardia[68]. Impaired conductivity was seen in 39.58±4.87% of the cohort, showing incomplete right-side bundle block. Comparisons over time (8 year to 10-11 years) showed that impaired conductivity increased from 35.6% to 39.6% ($p<0.001$). Polarization impairments were evident on 79.98±4.75% of the cohort, with “flattening of T-wave voltage in most leads, diphasic T-wave or a symmetric acuminated apex, more than 1 mm down shift of ST-segment from isoline or a more than 1.5 mm up shift”[68]. These changes were statistically different at 10-11 years follow-up, with an increase compared to the beginning of the study (56.8% to 79.9%, $p<0.001$). Systolic index rise and left ventricular hyperfunction were seen in 18.39±4.59% and 14.93±4.35% of the children and adolescents examined, respectively.

Kostenko, T.A.[68] also conducted examinations using radioelectrocardiography revealed decrease in adaptation to physical exertion in 56.41±5.88% of the children and adolescents, and PWC-170 test showed a decrease in physical ability in 48.43±5.93% of the children and adolescents. The investigator also evaluated the cerebral “homodynamic” (hemodynamic) of the children and adolescents in the study. The author’s findings indicate changes in the vascular tone in internal carotid and vertebrobasilar arteries (85.30±4.20%), arteriolar hypertonus (41.52±5.85%), unstable vascular tone (26.87±5.42%), difficulty in venous back flow (38.81±5.95%), asymmetry of pulse blood filling (40.23±4.88%), and decrease of pulse filling of the brain (20.91±4.83%)[68]. Comparison through the years showed an increase in cerebral vascular tone of 1.2 times (73.2% to 85.3%, $p<0.001$). Arterial hypertonus and venous backflow difficulty both decreased over time by 1.3 times from 52.5% to 41.5% ($p<0.001$), and from 52.5% to 38.85% ($p<0.001$), respectively. Lastly, the author performed echocardiography tests on the children at the different study periods and found that only 14.9±4.45% of the cohort did not show cardiac changes, in accordance to the other tests, the majority of the children and adolescents affected by the Chernobyl accident show progression of cardiovascular disease. Structural abnormalities were evident with single aberrant chords in ventricular cavities (in 38.8±5.9%), multiple aberrant chords (in 5.00±2.20%), abnormalities caused by connective tissue dysplasia and dysplastic cardiopathies (in

43.3±6.1%), evidence of valvular prolapse (in 49.3±6.1%), dilation of left ventricular final diastolic diameter (in 32.8±5.75%), transversal diameter of the aortic root (in 29.6±5.4%), and a decrease in both pump function and myocardial contractility (65.7±5.8% and 61.2±5.9%, respectively)[68]. Additionally, the investigator measured other cardiovascular parameters using the echocardiography tests, which further proved changes in contraction and pump function as well as cerebral hemodynamic changes that lead to progression of disease.

Reproductive Health

One article focused on reproductive health and examined fertility in women who were evacuated within the first 3 days of the disaster compared to women who lived in contaminated areas and women who lived in uncontaminated areas. Dubchak, A.E.[69] studied a total of 1221 women ages 19 to 40 years old between 1987 and 2000. Hormone levels were determined by radioimmunoassay and vaginal lining was examined by bacterioscopic and bacteriological methods[69]. The author reported an overall increase in morbidity, specifically, gynecological morbidity of 81% and 89.5% in women evacuated and women from contaminated areas, respectively between the years of 1986 and 2000. An increase of inflammatory disease of internal sexual organs was also found in 67.3% of evacuated women and 88.6% of women from contaminated areas. Over time, the inflammatory diseases resulted in anatomical and functional changes in the reproductive system of the women[69].

Immune and other blood related disorders

Dubchak, A.E.[69] also examined the cohort of women from evacuated, contaminated, and uncontaminated areas for immunological disorders. The author's findings include changes in the cellular link of immune response[69]. Women who remained living in contaminated areas had lower levels of CD3+ compared to both women who evacuated and those in uncontaminated areas (40.4±1.3% vs. 51.3±1.5% and 60.4±1.9%, respectively). Additionally, they had lower levels of CD16+ and decreased phagocytic activity of peripheral blood neutrophils.

Frolova, N.S. and colleagues[61] also conducted immunological evaluations in 13 patients. Compared to controls, liquidators showed a decrease in lymphocyte number (29.36±2.84% and 35.52±0.89%, $p<0.05$), T-lymphocytes CD2+ -phenotype (62.00±2.25%, 74.62±1.47% and 0.98±0.10, 1.54±0.08x10^9/1, $p<0.001$), CD3+ - phenotype (51.15±2.14, 68.76±1.54% and 0.70±0.09, 1.40x0.08x10^9/1, $p<0.001$). Humoral immune status in liquidators was different compared to controls. Liquidators showed an increase in circular immune complexes (at 123.46±12.26 vs. 66.62±3.84 arbitrary units). The authors also reported a decrease in phagocytic index as well as phagocytic number compared to controls (59.83±5.56 vs. 81.48±2.10%, and 6.63±1.19 vs. 13.62±0.96, respectively).

Discussion

Together, the studies found in the non-English literature continue to indicate to a decrease in health for those who were victims of the Chernobyl Disaster. The long-term effects of the accident are

evident in multiple studies carried out in children and adults in Belarus, Ukraine, and the Russian Federation. The preceding studies focused on neuropsychological consequences, well-being, suicide, CVD, reproductive health, and immune and other blood-related disorders. Our team was unable to review studies relating to respiratory diseases due to lack of access to full text of the articles, although several studies did indicate a high morbidity level among victims due to respiratory diseases. As many as 26 articles were found during our search of non-English literature that are potentially relevant to this review and focus on this topic.

The literature suggests that survivors of the accident suffered neuropsychological consequences that decrease their quality of life. Nyagu, A.I. and colleagues'[60] study in 1999 involved a battery of psychological tests and examinations with electroencephalography that revealed and confirmed a worsening of the brain and mental state of liquidators of the Chernobyl disaster. Liquidators exhibited higher indices of depression, anxiety and negative symptoms that hinder they quality of health and had distressing outcomes. Patients in the study by Nyagu, A.I. and colleagues[60] who were part of the clean-up efforts at Chernobyl had different EEG patterns that attest to the negative consequences of the irradiation, even at low doses. Nyagu, A.I. and colleagues[60] claim that while age, psychological stress, cerebrovascular pathology and duration of work influence psychophysiological disorder; the absorbed dose of radiation has a major contribution to the disorders. Khomazjuk, I.N. and Goncharenko, L.I.[63] confirm a higher frequency of hysteria, depression, hypochondria, and psychoasthenic states of liquidators with hypertension compared to controls. Frolova, N.S. and colleagues[61] concluded that 12-14 years after the accident, all liqidators in the study had changes in mental state and showed "neurological disturbances". Tabachnikov, S.I. and colleagues'[62] study also concluded that their findings indicated non-psychotic depressive disorders in individuals victims of the Chernobyl disaster, with over 80% of participants scoring anxiety levels of 52-56 points in the SAN scale.

The overall well-being of individuals who survived the accident, but were affected by it either psychologically or physically, seems to have dimished. Studies focusing on quality of life and well-being suggest poorer self-reported meantal and physical health, while studies on overall morbidity and mortality for those affected by the disaster compared to those who were not affected indicate higher levels of disability among those affected. Ipatov, A.V. and colleagues[64] attempted to understand the consequences of the Chernobyl disaster on the children of Ukraine, examining reports to estimate the number of children suffering from disabilities in different provinces. Findings from this study indicate that children from 6 provinces where survivors of the Chernobyl accident reside have indexes that exceed the averages of the rest of the Ukraine. Furthermore, children between 14 and 15 years of age, who were born in 1986 and 1987, presented with the highest levels of disability. Khomazjuk, I.N. and Goncharenko, L.I.[63] also found a decreased quality of life and physiologic changes that correlate with disease severity and duration. Yakovlev, P.A. and colleagues[65] in 2005 studied children who were born to father-liquidators compared to those who were not born to liquidators and those who lived in non-contaminated areas. Their findings indicate that the level of contamination of the father was a greater influence of children's well-being than living conditions, even living contaminated areas. The descriptive studies conducted by both Kharkovenk, R.V.[67] and Korytskyy G. I.[66] both speak to the health effects burdening the children and adults who were affected by the Chernobyl disaster, as well as the need for

continuous medical surveillance and care for these individuals. More children are suffering from respiratory diseases and cardiovascular disease among others. The studies indicate poor, overall well-being for the youth affected by the accident. Over time this deterioration progresses as they reach adulthood. The studies suggest continuance of high levels of morbidity and disability in the future adult population. Suicide was also a topic studied by Tabachnikov, S.I. and colleagues[62]. Their study found that liquidators of the Chernobyl accident displayed a higher risk of suicidal ideology and behavior ranging from suicidal ideas to action and uncommitted suicides. Prevalence of suicidal ideas was high at 92.8% and uncommitted suicides were recorded in about 9% of the participants.

Studies indicate CVD as a possible effect of the Chernobyl disaster. Kostenko, T.A.'s[68] work in 2005 focused on CVD and the Chernobyl disaster. The findings indicate that exposed children from the Zhytomir area showed "progressive unfavorable changes in functional condition of myocardium homodynamic" [68]. Khomazjuk, I.N. and Goncharenko, L.I.[63] found that hemodynamic changes, decrease of physical capacity and heart hypertrophy were more pronounced in victims of the Chernobyl disaster that had hypertension compared to those that did not present with hypertension. Higher frequency of psychological disturbances was also evident in the victims with hypertension.

Reproductive health and the immune system seem to be affected by the radiation exposure due to the Chernobyl disaster. Dubchak, A.E.[69] studied reproductive health and examined reproductive organ changes, as well as immunological and hormonal changes in 3 groups of women. Taken together, the findings suggest that the overall increase in gynecological morbidity and changes in reproductive function speak to a combination of the effects of low doses of radiation and stress. Frolova, N.S. and colleagues[61] also looked at immune status of liquidators and found decreased levels of lymphocytes, T-lymphocytes (CD2+ and CD3+ phenotypes, as well as phagocytic neutrophil activity compared to controls. The liquidators also had increased levels of hmoral immune complexes, speaking to a change in immune status for those exposed to the Chernobyl disaster.

Table 12: Non-English Literature: Neuropsychological Consequences

Non-English Literature Findings: neuropsychological consequences				
Reference	Source Description	Country, Period, Sex	Size (N), Type, Age (yrs)	Results
Frolova, N.S., et al. 2005	Neurological and immunological investigation 12-14 years after the Chernobyl disaster of liquidators.	1998-2000	105 liquidators, ages 33-61 years old. Control group included 48 healthy male individuals ages 22-45 years old.	• Asthenic syndrome= 65.7% of liquidators o Asthenic syndrome included: general cerebrogenic and somatocerebrogenic characteristics o Somatic pathology (chronic gastrointestinal diseases, arterial hypertensive disease, ischemic heart disease, chronic pyelonephritis, and deformity osteoarthrosis) developed in 67.6% of cases • Disseminated organic neurological symptomatology= 64.7% of liquidators • root or reflectory symptoms of spine osteochodrousis= 67.6% of liquidators • polyneuropathy= 16.19% of liquidators • dyscirculatory encephalopathy= 72.3% of liquidators • cerebral cyst adhesive arachnoiditis= 18% of liquidators
Khomazjuk, I.N. and Goncharenko, L.I., 2005	Examined neuropsychological disorders in LCAS participants who were liquidators with hypertension compared to LCAS participants without hypertension. Scales used for neuropsychological assessment included: • Memory rating scale of the Chernobyl accident event (IES)-	Ukraine	600 LCAS participants from 1986-1987; adults with average age of 48.8±0.8 years	• MMPI rank less than 10 evident in 17% of cases • MMPI rank exceeding 30 was evident in 9% of cases • 3% of patients thought they could not deal with negative senses • Evacuated people from Pripyat had more expressed negative memories compared to trained employees at the CNPP= 27.9±3.1 vs. 11.1±1.5 ($p<0.01$) • Average integral mark decreased by

	PTSD • MMPI-SMOL • Quality of Life assessed by medical and social questionnaires Clinical assessment included: • 24-hr monitoring of arterial pressure • echo • dopplercardiometry • veloergometry			7.2 over time (p<0.05) • Control group had average internal mark of 9±1.1 (11 marks less than LCAS participants with hypertension, p<0.05) • Integral mark value at complicated hypertension was higher (23.6±2) compared to value at absence of complications (18±1.9), p<0.05 • Average integral marks for LCAS participants with hypertension vs. control group (based on SMOL test): o Hypochondria= 69.6±2.1vs. 63.3±1.4 (p<0.05) o Depression= 62.7±1.8 vs. 61±2.4 (p>0.05). Depression average integral mark was significantly different for those with hypertension duration greater than 10 years compared to controls. o Hysteria= 71.2±1.8 vs. 54±2.4 (p<0.01) o Psychopathia= 51.7±2.2 vs. 54.2±2.1 (p>0.05) • Correlation between the PTSD mark and SMOL scales (1-3) were evident: o Scale 1= +0.41 (p<0.001) o Scale 2= +0.37 (p<0.05) o Scale 3= +0.39 (p<0.01) • Integral mark exceeding 70 was not evident in the control group • Personality types: o 6 categories identified: hypochondriacal, depressive, hysterical, psychoasthenic, mixed, and indefinite o Moderate hypertension was evident in all categories (highest among those classified as hypochondriacs

				and mixed-type personality at 93.7 and 92.7%, respectively)
Nyagu, A.I. et al., 1999	Psychophysiological examination of liquidators of the Chernobyl accident, including those who were diagnosed with ARS, and comparison with other groups exposed to radiation as well as healthy controls. Neuropsychological evaluation included: • Brief Psychiatric Rating Scale (BPRS) • Scale for the Assessment of Negative Symptoms (SANS) • Screening Schedule • PTSD Scales: Impact of Events Scale (IES) and Arousal Scale of PTSD (IDA) • Self-Rating Depression Scale (SDS) • General Health Questionnaire (GHQ-28) • Adapted and validated MMPI • Working capacity diagnostic method (test of E. Landolt) • Wechsler Adults Intelligence Scale (WAIS) • Computerised EEG (cEEG) • Visual Evoked	Ukraine, 1986-1987, males	200 patients and controls divided into 6 categories: 1. Diagnosed with ARS: n=70 2. 80 Liquidators from CNPP (divided into 2 sub-groups): group A (those on-site < 3 months) n=37 and group B (those on-site 3+ yrs) n=43 3. Healthy control n=15 4. Patients with dyscirculatory encephalopathy n=15 5. Veterans of the Afghanistan war with PTSD n=20	• Liquidators and ARS groups showed high prevalence of: o Headaches: 86% and 83% o Memory deterioration: 76% and 77% o Limb pain: 69% and 74% o Sensoric-algetic disorders: 85% and 93% o Autonomic disorders: 90% and 96% • Liquidators were statistically different from ARS patients in prevalence of: o Paroxismal state: 47% vs. 66% ($p<0.025$) o Diffusive microfocal neurological signs: 44% vs. 64% ($p<0.025$) • Vertigo and Fatigue prevalence in liquidators and ARS groups: 51% and 53%; 66% and 69%, respectively • Depressive mood and irritability prevalence in liquidators and ARS groups: 32% and 31%; 44% and 41%, respectively Mental State: • BPRS scale: Anxiety index for liquidators was significantly different compared to healthy control (3 ± 0.2 vs. 1.1 ± 0.1; $p<0.05$), and slightly higher than patients with ARS • BPRS scale: Emotional withdrawal index for liquidators was significantly different compared to healthy control (2.2 ± 0.2 vs. 0.5 ± 0.1; $p<0.01$), and slightly lower than patients with ARS • BPRS scale: Depressive mood index for liquidators was significantly different compared to healthy control

	Potentials			(3.6±0.2 vs. 1.2±0.2; p<0.01), and slightly higher than patients with ARS Negative Psychopathological symptoms: • Indices of the scale for the assessment of negative symptoms (SANS): liquidators vs. healthy control group o Affective flattening or blunting: 2.1±0.2 vs. 0 (p<0.01) o Alogia: 1.9±0.2 vs. 0 (p<0.05) o Avolition-apathy: 2.5±0.2 vs. 0 (p<0.01) o Anhedonia-asociality: 2.6±0.2 vs. 0 (p<0.01) o Attention: 2.3±0.2 vs. 0 (p<0.01) • Screening Schedule: 62% of irradiated patients at an increased risk to develop severe mental disorders 100% of Chernobyl survivors experienced psycho-emotional stress due to the accident (PTSD): • IES: average score for liquidators compared to ARS patients was 34.6±6.7 vs. 28.4±5.6, respectively • Memory of the disaster and associated arousal evident in 27% of liquidators and 11% of ARS patients • SDS: o Minimal-mild AND moderate-marked depression: 56% of liquidators and 58% of ARS patients o Severe to extreme depression: 21% of liquidators and 10% of ARS patients • GHQ-28: all survivors rated their mental and physical health worse

				than usual MMPI-profile: • ARS and liquidators (irradiated groups) vs. healthy control: o Irradiated groups more pronounced stress and personality disadaptation than control group o Psychosomatic predisposition in irradiated groups (asthenic type of reactions, depression, hypochondriac and paranoiac symptoms) o Statistically significant increase in schizophrenia hypochondria, paranoia, epilepsy and odd sensoric perception in irradiated groups compared to controls ($p<0.01$) EEG and Visual Evoked Potentials: • EEG patterns significantly different for irradiated groups compared to controls (ARS and liquidators vs. healthy controls): o EEG pattern organized with α-activity dominance: 0 vs. 27% vs. 80% ($p<0.001$ relative to ARS patients) o EEG pattern hypersynchronic: 10% vs. 9% vs. 20% (NS) o Flat polymorphus: 83% vs. 69% vs. 0 ($p<0.001$ for control relative to ARS group only) o Disorganized with α-activity dominance: 3% vs. 12% vs. 0 (NS) o Disorganized with δ-activity dominance: 4% vs. 10% vs. 0 o Laterality of abnormal activity

				(ARS vs. liquidators): ▪ Bilateral: 20% vs. 7% vs. 20% (NS) ▪ Left-hemispheric: 57% vs. 31% (p<0.001) ▪ Right-hemispheric: 23% vs. 35% (NS) • Computerized EEG (ARS and liquidators vs. control groups): o Irradiated patients had increase in delta and beta power and a decrease in theta and alpha power (Δ 1-4 Hz; β >12-32 Hz; θ>4-7 HZ; α >7-12 Hz) o Short term CNPP stay difference between dose: Δ-power lower in <0.3 Gy vs. >0.3Gy (p<0.001); α-power higher for <0.3Gy vs. >0.3Gy (p<0.001); β-power higher for <0.3 Gy vs. >0.3Gy (p<0.05); o Long term CNPP stay difference between dose: Δ-power lower in <0.3 Gy vs. >0.3Gy (p<0.001); α-power higher for <0.3Gy vs. >0.3Gy (p<0.001) o Among those with dose of <0.3 Gy difference in stay: Δ-power lower in < 3 months vs. 3-5+yrs (p<0.05) o Among those with dose of >0.3 Gy difference in stay: β-power lower in < 3 months vs. 3-5+yrs (p<0.05) • Visual Evoked Potentials (ARS vs. Liquidators vs. healthy control): o VEP latency, ms (p-value is probability compared to ARS):

				▪ $P_{100}O_2$: 82.0±1.1 vs. 89.2±1.1 (p<0.01) and 96.8±1 (p<0.01) ▪ $N_{145}O_2$: 128.1±1.5 vs. 138.2±1.5 (p<0.01) and 147.0±1.6 (p<0.01) ▪ $P_{200}O_2$: 237.2±1.7 vs. 221.4±1.7 (p<0.01) and 208.0±1.6 (p<0.01) o VEP amplitude, μV(p-value is probability compared to ARS): ▪ $P_{100}O_2$: 4.2±0.1 vs. 3.2±0.2 (p<0.01) and 2.6±0.1 (p<0.01) ▪ $N_{145}O_2$: 7.6±0.1 vs. 5.6±0.3 (p<0.05) and 4.2±0.1 (p<0.01) ▪ $P_{200}O_2$: 5.9±0.2 vs. 4.9±0.3 (p<0.05) and 5.6±0.3 (NS)
Tabachnikov, S.I. et al., 2005	Clinical, psychological, electrophysical and biochemical examination among CNPP liquidators. Psychological scales used included: • Hamilton scale • Spielberg scale • Zung self-estimated scale of depression • Test for an assessment person stress resistant • Rheoencephalographic method • Electrophysiological and biochemical procedures	Kiev, Ukraine, males and females	152 liquidators: 110 men and 42 women, ages 40-59 years old (50-59 years old for men and 40-49 years old for women)	• Non-psychotic depressive disorders: o Astheno-depressive: 38.2% o Depressive: 27.6% o Depressive hypochondriac: 11.2% o Anxiety-depressive: 12.5% o Depressive-phobic: 10.5% Somatoneurologic pathology (selected diseases): o Idiopathic hypertension: 75 patients (49.3%) o Ischemic heart disease: 55 patients (36.2%) o Dyscirculation encephalopathia: 91 patients (59.9%) o Cerebral arteriosclerosis: 44 patients (28.9%)

				• Trends of rapid exhaustion of mental activity: o In organic depressive disorder: F=06.32 o In organic emotional-labile disorder: F=06.6 • SAN scale: Anxiety level= 52-56 points in 82.2% of patients Biochemical examination: • Disbalance between levels of noradrenalin, dofaminum, heterochronic changes in adrenaline excretion, increasing levels of serotoninum in the blood, and disbalance of lipid oxidation and endogenous intoxication are present in liquidators. • Level of malonic dialdehyde and medium-sized molecule among those with depressive disorders of organic nature are higher than those with psychosomatic disorders ($p<0.05$) • Level of malonic dialdehyde and medium-sized molecule among hose with anxiety-depressive disorders are higher than those with psychosomatic disorders ($p<0.05$)
NS: not statistically significant				

Table 13: Non-English Literature: Reproductive Health

Non-English Literature Findings: reproductive health				
Reference	Source Description	Country, Period, Sex	Size (N), Type, Age (yrs)	Results
Dubchak, A.E., 2005	Clinical and para-clinical examinations including examinations with therapeutist, endocrinologist, oculist, neurologist, and other specialist.	Ukraine, 1987-2000, Females	1221 women ages 19-40 years old.	General morbidity apparent in: • 70.5% of women evacuated • 66% of women living in contaminated territories Gynecological morbidity: • 81% of women evacuated

	Tests conducted: • Hysterosalpingography • Digital subtraction videometrosalpingography • Ultrasonic monitoring • Radioimmunoassay for hormone levels (LH, FSH, PRL, estradiol, progesterone, testosterone, TTH, T3, T4, ACTH, cortisol, anti-TPO, and anti-TG) • Flowcytometry, immunem-monitoring kit and Simulet Software were used to determine lymphocyte subsets in whole blood • IgG, IgA, IgM, sIgA and lisozyme levels were analyzed using immunodiffusion • Antisperm antibody (ASA) was determined using Isojima method • Vaginal lining examined by bacterioscopic and bacteriological methods • Changes in ovary and uterine tubes tissue studied			• 89.5% of women living in contaminated territories Increase in inflammatory disease of internal sexual organs: • 67.3% of women evacuated • 88.6% of women living in contaminated territories Disorders of menstrual cycle, benign tumors in ovaries: • 12.3% of women evacuated • 9.3% of women living in contaminated territories Pathologies of the cervix: • 27% of women evacuated • 20.5% of women living in contaminated territories Uterine leiomyoma, genital endometriosis: • 12.8% of women evacuated • 10.9% of women living in contaminated territories For evacuated women, blood levels of estraidol were highly correlated with: • hypermenstrual syndrome: $r=0.62$, $p<0.05$ • hyperplasia of endometrium: $r=0.52$, $p<0.05$

Table 14: Non-English Literature: Well-Being

Non-English Literature Findings: well-being				
Reference	Source Description	Country, Period, Sex	Size (N), Type, Age (yrs)	Results
Khomazjuk, I.N. and Goncharenko, L.I., 2005	Examined neuropsychological disorders in LCAS participants who were liquidators with hypertension compared to LCAS participants without hypertension. Scales used for neuropsychological assessment included: • Memory rating scale of the Chernobyl accident event (IES)-PTSD • MMPI-SMOL • Quality of Life assessed by medical and social questionnaires Clinical assessment included: • 24-hr monitoring of arterial pressure • echo • dopplercardiometry • veloergometry	Ukraine	600 LCAS participants from 1986-1987; adults with average age of 48.8±0.8 years	• Quality of life study showed integral marks for LCAS participants with hypertension= (-) 15.8±1.2 vs. integral marks for the control group= + 5.1±0.5 ($p<0.05$) • Quality of life integral mark had a significant difference between those with hypertension up to 5 years compared to those with hypertension 5-10 years, (-) 14.1±1.3 vs. (-) 17.7±0.9 ($p<0.05$) • Among study group, difference in decrease of Quality of Life due to: o Necessity to receive treatment= 25% for those with hypertension up to 5 years vs. 75% for those with hypertension between 5-10 years. • Correlation between the Quality of Life mark and SMOL scales (1-3) were evident (lower Quality of Life marks): o Scale 1= -0.43 ($p<0.001$) o Scale 2= -0.53 ($p<0.01$) o Scale 3= -0.41 ($p<0.01$)

Ipatov, A.V. et al., 2004	Examined causes of disability among children in provinces across the Ukraine. Reviewed and analyzed information from the Ukraining state stataistic reporting of pediatric service (form #16) and Ukrainian state statistic reporting on medical-social expert commissions (form #14)	Ukraine, 2001, males and females	Children ages 16 years old and younger	• Overall disability due to disease of blood and hemopoietic organs in Ukraine: 1.9 per 10,000 children o Of provinces studied: highest was Cherkassy province at 2.6 per 10,000 children (an excess of 36.8% compared to overall average in Ukraine) and lowest was Chernygov at 1.6 per 10,000 children • Overall disability due to mental and behavioral disorders in Ukraine: 27 per 10,000 children (including mental retardation= 22.8 per 10,000 children) o Overall (for provinces studied): highest was Chernygov province at 37.1 per 10,000 children (an excess of 37.4% compared to overall average in Ukraine) and lowest was Volyn at 16.9 per 10,000 children • Overall disability due to diseases of the nervous system in Ukraine: 39.8 per 10,000 children (including cerebral paralysis= 23.1 per 10,000 children) o Overall (for provinces studied): highest was Rovno province at 54.6 per 10,000 children (an excess of 37.2% compared to overall average in Ukraine) and lowest was Chernygov at 31.5 per 10,000 children • Overall disability due to diseases of the respiratory system in Ukraine: 8.8 per 10,000 children (including bronchial asthma= 7.9 per 10,000 children) o Of provinces studied: highest

				was Chernygov province at 11.1 per 10,000 children (an excess of 26.1% compared to overall average in Ukraine) and lowest was Volyn at 3 per 10,000 children • Among 14-15 year olds only, difference percentage of average indexes (examined provinces vs. other provinces in Ukraine) for selected diseases: o Diseases of blood and hemopoietic organs= +38.2% o Mental and behavioral disorders= - 10.1% o Diseases of the nervous system= +7.5% o Diseases of the respiratory system= +16.3%
Yakovlev, P.A. et al., 2005	Estimate of rate of sickness for children using medical charts up to January 1, 2004.	Oryol region, Ukraine, 2004, males and females	265,000 medical charts from the medico-dosimetric register for children born to liquidators and 131,800 children whose parents were not liquidators and reside in the "clean" districts of Oryol region	• Sickness rate in children born to liquidators is 1.4 times higher than regional data (2,626.4 vs. 1,860.9) • Increasing sickness rate among children of liquidators up to 2003: o 1991= 862.5 per thousand o 1996= 1537.6 per thousand o 2000= 1607.4 per thousand o Decreased at 369.3 in 2003 • Disease incidence for children in contaminated areas by radio nuclides, and not born to liquidators (rate is lower by 388.2 than children born to liquidators): o 1991= 473.6 per thousand o 1996= 728.6 per thousand o 2000= 713.5 per thousand o 2003= 861.8 per thousand • Disease incidence in "clean" areas: o 1991= 1128.7 per thousand o 1996= 1163.6 per thousand o 2003= 1407.1 per thousand

				• Major cause of sickness for children born to liquidators and those in the general population was respiratory disease= 788.7 (relative density of 63.7%), in the region 893.2 • Blood illnesses= 2.7 times higher in 2003 compared to 2000 (11.3 vs. 4.1, respectively) • Sickness by parent radiation dose: o Dose: Over 25P (radiation dose measurement unit from authors)= majority of children with disease are 11-14 years old (3.1 registered illnesses) o Dose: 20-25P= mostly children between 15-16 years old (all ages: 2.2 registered illnesses; only 15-16 year olds in this group: 3.3 registered illnesses) o Dose: 10-20P= mostly in children 15-16 years old (all ages 2.2 registered illnesses; only 15-16 years old in this group: 1.8)
Korytskyy, G.I., 2013	Examined the causes of morbidity and disability in children affected by the CNPP accident based on annual examinations. Additionally, a comparative analysis was conducted to understand morbidity for children affected by Chernobyl compared to children who were not affected by the accident.	Ternopil region, Ukraine, 2003-2011, males and females	All children with the status of "victim of CNPP disaster" and children in the region who were not affected by the CNPP accident	• Overall number of children classified as "victims" of the CNPP accident (overall children population in the region decreased by 60,848 due to new classification as adults): o 2003= 8,994 o 2004= 8,162 o 2005= 8,184 o 2006= 8,407 o 2007= 8,088 o 2008= 7,749 o 2009= 7,565 o 2010= 7,274 o 2011= 7,222 • Number of children ("victims") treated in the hospitals decreased

				from 1,726 in 2003 to 1,231 in 2011 • Number of children ("victims") treated on outpatient conditions decreased from 5,349 in 2003 to 4,419 in 2011 • Number of children ("victims") treated in sanatoria and health resorts decreased from 2,106 in 2003 to 793 in 2011 • Number of children ("victims") classified as healthy decreased from 1,456 in 2003 to 1,391 in 2011 o Annually, the number of children found healthy in the region, among those classified as "victims" varies within 11-19% • Children "victims" are 1.8 to 2.5 times more overall morbidity than children who are not classified as victims of the accident (with a trend of annual growth)
Kharkovenko, R.V., 2013	Examine causes of morbidity for victims of the CNPP accident in the Vinnitsa region, Ukraine from medical records.	Vinnitsa region, Ukraine, 2003-2012, males and females	All victims of the CNPP accident and overall population in the region. Groups: • Liquidators • Evacuees • Residents of contaminated areas • Affected children • The whole region	• Overall number of people affected by the CNPP accident in Vinnitsa region (selected years): o 2003: ▪ Liquidators= 4,686 ▪ Evacuees= 532 ▪ Residents of contaminated areas= 82,820 ▪ Affected children= 23,419 o 2012: ▪ Liquidators= 4,485 ▪ Evacuees= 579 ▪ Residents of contaminated areas= 68,805 ▪ Affected children= 18,371

				• Victims classified as "healthy" (selected years): o 2003: ▪ Liquidators= 7.54% ▪ Evacuees= 6.06% ▪ Residents of contaminated areas= 22.72% ▪ Affected children= 25.84% o 2012: ▪ Liquidators= 0.4% ▪ Evacuees= 1% ▪ Residents of contaminated areas= 17.6% ▪ Affected children= 21.2% • Overall incidence of disease causes (up to 2011): o 1st: circulatory diseases (45% due to hypertension) o 2nd: respiratory diseases o 3rd: digestive system diseases o 4th: endocrine system diseases o 5th: muscular system diseases • Overall incidence of disease causes (2012): o 1st: respiratory disease= 33% o 2nd: genitourinary system= 10.6% o 3rd: circulatory diseases=10.5% • In the adult victims only, circulatory diseases caused 77.3% of all deaths • 2003-2012 proportion of healthy individuals: o Liquidators: decreased by 18.85 times ($p<0.001$) o Evacuees: decreased by 6

				times

Table 15: Non-English Literature: Suicide

Non-English Literature Findings: Suicide				
Reference	Source Description	Country, Period, Sex	Size (N), Type, Age (yrs)	Results
Tabachnikov, S.I. et al., 2005	Clinical, psychological, electrophysical and biochemical examination among CNPP liquidators. Psychological scales used included: • Hamilton scale • Spielberg scale • Zung self-estimated scale of depression • Test for an assessment person stress resistant • Rheoencephalographic method • Electrophysiological and biochemical procedures	Kiev, Ukraine, males and females	152 liquidators: 110 men and 42 women, ages 40-59 years old (50-59 years old for men and 40-49 years old for women)	Suicidal ideology: • Ideas: 141 patients (92.8%) • Statements: 62 patients (40.8%) • Intention: 42 patients (27.6%) • Action: 18 patients (11.8%) • Uncommitted suicide: 14 patients (9%)

Table 16: Non-English Literature: CVD

Non-English Literature Findings: CVD				
Reference	Source Description	Country, Period, Sex	Size (N), Type, Age (yrs)	Results
Khomazjuk, I.N. and Goncharenko, L.I., 2005	Examined neuropsychological disorders in LCAS participants who were liquidators with hypertension compared to LCAS participants without hypertension.	Ukraine	600 LCAS participants from 1986-1987; adults with average age of 48.8±0.8 years	• Average daily SAP (systolic arterial pressure) variation was ≤ 5.1 mm Hg among all personality categories (excluding those in the indefinite category) • Average daily DAP (diastolic arterial pressure) was slightly higher for the

	Scales used for neuropsychological assessment included: • Memory rating scale of the Chernobyl accident event (IES)-PTSD • MMPI-SMOL • Quality of Life assessed by medical and social questionnaires Clinical assessment included: • 24-hr monitoring of arterial pressure • echo • dopplercardiometry • veloergometry			mixed-type (98.1±2.4) and overall variation was ≤ 5.2 mm Hg among all personality categories (excluding indefinite category) • SAP and DAP time index percentages were highest among the mixed-type personality compared to other groups (87.5±4.3%, p<0.01 and 75±2.2%, p<0.01, respectively) • Thickness of interventricular wall to diastole (TIVWd) and thickness of aortic ventricle back wall to diastole (TAVBWd) variation were ≤ 1.1 mm for all personality categories • Both TIVWd and TAVBWd were highest among the mixed-type personality category • Power threshold load at veloergometry was highest among depressive and lowest among the mixed-type personality category (102.2±4.5 W and 93.1±3.8 W, respectively)
Kostenko, T.A., 2005	Understand the influence of radiation on the cardiovascular system of children victims of the CNPP accident. Examination included: • ECG recorded on multichannel electrocardiographs • RECG with a dosed exertion loading on a national veloergometer • Rheoencephalograms (REG) • PWC-170 test • Echocardioscopy	Zhytomir area, Ukraine, 1994-1997 (8-11 years after the accident), males and females	Children and adolescents evacuated from contaminated zones in Zhytomir area, after living there for 4-5 years after the accident.	• By 10-11th year after the CNPP accident, 50% of cohort had myocardial bioelectric activity changes: o Automation functional disorder o Sinus arrhythmia o Bradycardia and single cases of tachycardia • Conductivity impairments= 39.58±4.87% of cohort • Polarization impairments= 79.98±4.75% of cohort • Myocardial functional capacity drop= 18.93±4.59% of cohort • Left ventricular hyperfunction= 14.93±4.35% of cohort

	(Echo-CS) • Doppler echocardiography			• Decrease in adaptation to physical exertion= 56.41±5.88% of cohort • Fall in general physical ability (per the PWC-170 test)= 48.43±5.93% • Alterations of vascular tonus in internal carotid and vertebrobasilar arteries= 85.30±4.20% of cohort • Arteriolar hypertonus= 41.52±5.85% of cohort • Unstable vascular tonus= 26.87±5.42% of cohort • Difficulty in venous back flow= 38.81±5.95% of cohort • Asymmetry of pulse blood filling= 40.23±4.88% of cohort • Decrease of pulse filling of brain= 20.91±4.83% of cohort • Increase of repolarization over time (8^{th}, 9^{th}, 10-11^{th} years): from 56.8% to 79.9% ($p<0.001$)= 1.4 times rise over time • 1.2 time increase in frequency of parameters such as impairment of cerebral vascular tonus over time (from 73.2% to 85.3%, $p<0.001$) • Decrease of arterial hypertonus incidence over time (from 52.5% to 41.5%, $p<0.001$) • Decrease in frequency of venous backflow difficulty over time (from 52.5% to 38.85%, $p<0.001$) • Absence of cardiac changes evident on 1/6 of cohort (14.9±4.45%) Incidence of: o Single aberrant chords in ventricular cavities= 38.8±5.9% of cohort o Multiple aberrant chords in ventricular cavities= 5±2.2% of cohort

				○ Dysplastic cardiopathies= 43.3≠6.1% of cohort ○ Valvular prolapsis= 49.3±6.1% of cohort ○ Dilation of left ventricular final diastolic diameter= 32.8±5.7% of cohort ○ Transversal diameter of aortic root= 26.9±5.4% of cohort • Decrease myocardial contractility= 61.2±5.9% of cohort

Table 17: Non-English Literature: Immune and Other Blood-Related Disorders

Non-English Literature Findings: Immune and other blood-related disorders				
Reference	Source Description	Country, Period, Sex	Size (N), Type, Age (yrs)	Results
Dubchak, A.E., 2005	Clinical and para-clinical examinations including examinations with therapeutist, endocrinologist, oculist, neurologist, and other specialist. Tests conducted: • Hysterosalpingography • Digital subtraction videometrosalpingography • Ultrasonic monitoring • Radioimmunoassay for hormone levels (LH, FSH, PRL, estradiol, progesterone, testosterone, TTH, T3, T4, ACTH, cortisol, anti-TPO, and anti-TG)	Ukraine, 1987-2000, Females	1221 women ages 19-40 years old.	Immunological results: • levels of CD3+ cells was lower in: ○ 51.3±1.5% for evacuated women ○ 40.4±1.9% for women living in contaminated territories • phagocytic activity of peripheral blood neutrophils decreased in both groups compared to index group: ○ 68.3±2.4% for evacuated women ○ 71.4±1.2% for women living in contaminated areas ○ 82.4±1.2% in index group • Levels of CD16+ were lower in both groups compared to index group ($p<0.05$) • Development of immunodeficiency at cellular (decrease in CD3+ and CD16+ cells and increase in CD19+ cells) and humoral (low levels of IgG and IgA) levels in:

	• Flowcytometry, immunem-monitoring kit and Simulet Software were used to determine lymphocyte subsets in whole blood • IgG, IgA, IgM, sIgA and lisozyme levels were analyzed using immunodiffusion • Antisperm antibody (ASA) was determined using Isojima method • Vaginal lining examined by bacterioscopic and bacteriological methods • Changes in ovary and uterine tubes tissue studied			o 34% of evacuated women o 46% of women living in contaminated territories • Hyperestrogenemia confirmed (42% of evacuated women) by development of: o Hyperplasia of endometrium= 20% o Submucous uterine myoma= 10% o Adenomyosis fo uterus= 13.3% • Levels of prolactinum: o 2 times higher in evacuated women compared to index group o 0.5 times higher in women living in contaminated territories compared to index group • Levels of cortisol and ACTH: o Higher in both groups compared to index group ($p<0.05$) o Hypercorticoidism in 74.6% of evacuated women (with sharp decline 1992-1993 and stabilization in last years) o For women living in contaminated territories, cortisol levels increased from 1989-1990 • Changes in ovarian stroma evident in evacuated women. Formation of polyp structures in epithelium evident in 78% of cases Sclerotic vascular changes in women living in contaminated trerritories was evident with 60% of women having atrophic lesions with mucous membrane adhesion and high expression of collagen type I in

				uterine tubes.
Frolova, N.S. et al., 2005	Neurological and immunological investigation 12-14 years after the Chernobyl disaster of liquidators.	1998-2000	105 liquidators, ages 33-61 years old. Control group included 48 healthy male individuals ages 22-45 years old.	• Liquidators' cellular level immune status compared to control group (decrease in levels for liquidators): o General lymphocytes= 29.36±2.84% vs. 35.52±0.89%, ($p<0.05$) o T-lymphocytes CD2+ phenotype= 62±2.25; 74.62±1.47% and 0.98±0.10; 1.54±0.08x10^9/1 ($p<0.001$) o CD3+ phenotype= 51.15±2.14; 68.76±1.54%; and 0.70±0.09; 1.40±0.08x10^9/1 ($p<0.001$) • Liquidators' humoral immune status compared to control group: o Increase in circular immune complexes= 123.46±12.26 vs. 66.62±3.84 arbitrary units o Decrease phagocytic index= 59.83±5.56 vs. 81.48±2.10% Decrease phagocytic number= 6.63±1.19 vs. 13.62±0.96

Table 18: Total Publications by Topic of Non-English Literature- No Access to Full Text

Topic	Number of references
Neuropsychological consequences	103
Well-being and overall health status	41
Suicide	1
CVD	26
Reproductive Health	16
Immune disorders & other blood-related disorders	57
Respiratory Diseases	26
Diabetes	1
Reports, reviews, and other articles with insufficient information to categorize	57

Table 19: List of Non-English Literature (No Access to Full Text Review): Neuropsychological Consequences

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Table 20: List of Non-English Literature (No Access to Full Text Review): Well-Being

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Table 21: List of Non-English Literature (No Access to Full Text Review): Suicide

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