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MONOGRAPHIC SECTION

A survey on lifestyle and level of biomarkers of environmental exposure in residents in Civitavecchia (Italy)

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**Components of the ABC Study Group are listed before the References*

Abstract

Background. The assessment of individual exposure to toxicants in industrially contaminated areas is difficult when multiple productions are active close to residential areas. Two thermoelectric power plants and a large harbor have been operating since the '60s in the area of Civitavecchia (North of Rome).

Methods. The ABC (Ambiente e Biomonitoraggio nell'area di Civitavecchia, Environment and Biomonitoring in Civitavecchia) program involved, in the period 2013-2014, residents in Civitavecchia and in the nearby municipalities (Santa Marinella, Allumiere, Tolfa and Tarquinia). They were randomly selected from the Municipal Register's data and their residence addresses were geocoded using GIS techniques. Biomonitoring of the following urinary metals, Sb, Be, Mo, Cd, Sn, W, Ir, Pt, Hg, Tl, V, Cr, Mn, Co, Ni, Cu, Zn, Rh, Pd, As were performed. Glucose and lipid metabolism, liver, renal, and endocrine function were evaluated through blood laboratory tests. Tests of lung function were also carried out as well as saturometry (oxygen rate in the blood with an illuminated sensor placed on the fingertip), anthropometric and blood pressure measurements. Information on individual characteristics, histories of exposure, such as the consumption of local food, occupational history, lifestyle and medical history were collected through a validated questionnaire. Samples of nails and hair were also collected. The biological material (blood, urine, nails and hair) was stored in a biobank for future analysis related to the possible mechanisms of biological damage. The study protocol received the approval of the local ethics committee.

Results. A total of 1177 residents were enrolled (58% female, 60% with a secondary or graduate school degree). No particular differences in metal concentrations based on the municipality of residence were observed. For arsenic, mercury, lead, and tungsten some differences between the two geographical areas were observed, probably due to different diet, lifestyle (*e.g.*, alcohol consumption, smoking, use of jewelry and piercings, tattoos, physical activity, hormonal and mineral supplements, and drugs), and occupational exposure.

Conclusions. The undergoing study on the association between biomarkers concentration and pollutants concentrations – estimated using a dispersion modeling approach, and adjusting for personal characteristics and concomitant other environmental exposure – could clarify the individual exposure of the residents in this industrial area.

Key words
- human biomonitoring
- metals
- industrially contaminated areas

INTRODUCTION

Civitavecchia (51 229 inhabitants as the 2011 national census) is an industrial town located along the northern cost of Rome (Lazio region, Central Italy). It has been a reason of concern for several years because of various sources of environmental contamination poten-

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tially affecting the residential communities: a large harbor, a cement factory, and three thermoelectric power plants. In addition, biomass burning is frequently used in the rural part for heating purposes.

In response to concerns expressed by community residents about the possible risks arising from the industrial plants, previous studies have been already carried out in this area to evaluate the health status of workers and residents in the area. A study among dockyard workers in the harbor published in 1985 showed an excess of lung cancer [1], lung cancer deaths were also significantly higher in a cohort of seamen than in the general population [2], and a cohort study among workers employed in one of the thermoelectric power plants showed an excess of lung cancer among those with a duration of exposure longer than 10 years [3]. An excess of mesotheliomas was also noted among workers of the power plants and among seamen. As for the resident population, the first investigation on the possible impact of air pollution in the area of Civitavecchia dates back to 1987 when an epidemiological survey was conducted among primary school children and a higher frequency of respiratory diseases and bronchial reactivity was detected among children of the Civitavecchia area compared with the reference group living in a rural area [4, 5]. A specific case-control study on lung cancer was conducted in 2004 to assess the role of occupational and environmental exposures. Smoking habits and occupational exposure to asbestos were associated with increased lung cancer risk (www.cuore.iss.it/fattori/progetto.asp). The first extensive study on mortality and morbidity of Civitavecchia residents was reported in 2006 with the analysis for the period 1997-2004. Excess risks of lung and pleural cancer among men, and bronchial asthma among adults and children were detected [6].

However, individual data about human exposure to contaminants from the different sources of pollution in this area are not available. Some of these pollutants, characterized by chemical and physical stability and potential toxicity, may contaminate soil, plants and animals, and thus enter the food chain. These pollutants are present in the tissues of the general population usually at relatively low concentrations, with a half-life of even several years. High concentrations in the body may be associated with health effects.

The aim of the ABC epidemiological program (Environment and Biomonitoring in Civitavecchia district – Ambiente e Biomonitoraggio nell'area di Civitavecchia) was to study the health status of the population, to describe the frequency distribution of the individual risk factors, and to evaluate indexes of possible contamination of toxicological significance.

METHODS

The study plants and the area of investigation

The harbor (241 000 m^2) has been traditional used for ferry traffic, merchant ships and tankers, only recently cruise ships also anchor there. Environmental surveys indicate that dusty materials (around 500 000 tons a year) are the main source of pollution from the harbor, causing increased dust dispersion in the air while the goods are transferred from buckets to trucks. Another source of pollution from the harbor is the traffic of heavy vehicles and ferries; ships and ferries use a large amount of fuel containing high sulphur levels (up to 2.9%), and producing substantial quantities of sulphur oxides and particulates.

Two thermoelectric power plants are located in the study area: Tor Valdaliga North (TVN) and Tor Valdaliga South (TVS). The power plant TVN is located about 5 km north west of the built up area, near TVS; it has been active since 1984 and produces 2640 MW of power, the plant has been converted into a coal-fired power plant in 2010. The power plant TVS is located about 4 km north-west of the built up area. It is active since 1964 as oil-fuelled plant and produces 1140 MW of power, it has been recently converted to a gas-fuelled plant. Emissions from the power plants include particles, nitrogen dioxide (NO2) and sulphur dioxide (SO2).

Sampling and enrolment of ABC study participants

All residents (18 years +) living in Civitavecchia and in the nearby municipalities (Santa Marinella, Allumiere, Tolfa and Tarquinia) at January 1, 1996 were enrolled by using the Municipalities Registries. For each subject personal data, address of residence, and date of emigration (immigration) were available. The population of the municipalities concerned was georeferenced using the ArcGIS program.

Among the residents a random sample of 2000 residents (35-69 years) was selected and invited to participate in the survey ABC. The sample, balanced by sex, is composed of 1200 residents in Civitavecchia, 200 in Tarquinia, 300 in Santa Marinella, 140 and 160 in Allumiere and Tolfa, respectively.

Figure 1 shows the study area, the industrial plants, and the spatial distribution of the residents and of the sample in Civitavecchia area.

Organization of the ABC study

Study participants received a letter of invitation to participate in the study. 1790 residents were contacted by telephone. 34% of contacted, however, refused to participate. A number of 1177 persons (66% of those

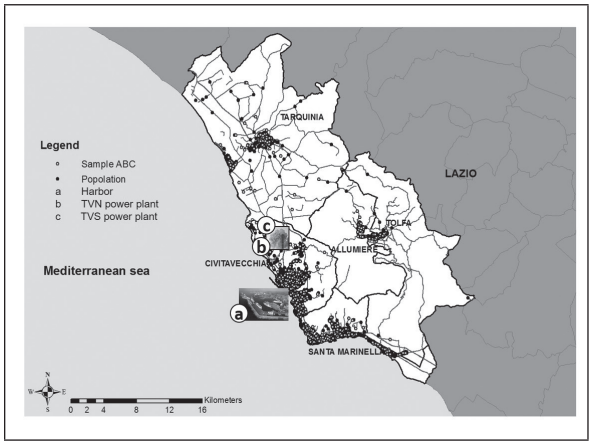

Figure 1
Study area, industrial plants, and distribution of residents.

contacted by telephone) agreed to participate. *Figure 2* describes the recruitment activities and the compliance of the ABC sample.

Biomarkers

Measuring the metal concentration in urine samples in biomonitoring studies, allows to assess the exposure to environmental pollutants of a given population. The measured metal levels reflect the amount that actually enters the body through all routes of exposure, ie ingestion, inhalation and skin absorption. The presence of a metal in the human body may be indicative of exposure, present and / or past, but this does not necessarily imply a negative effect on health nor an association with the onset of a disease. The selection of metals to be considered in the ABC study was driven by the specific pollution sources in the area and from published literature, in particular the National Health and Nutrition Examination Survey (NHANES) conducted on a large sample of people in the United States (www.cdc.gov/nchs/nhanes.htm) *(Table 1)*.

As indicated in the documents published by the American Conference of Governmental Industrial Hygienists (ACGIH) in 2006 and by WHO in 2012, blood has been considered as best biological matrix for the determination of lead, while the other metals were analyzed in urine.

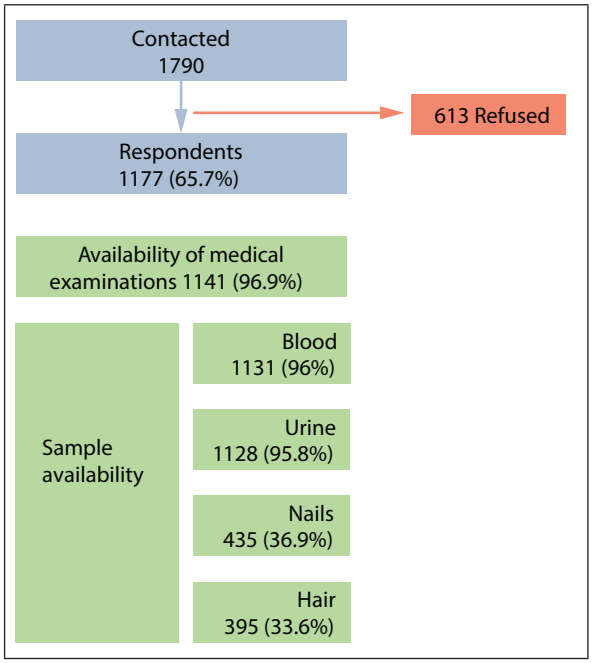

Figure 2
Flow chart of the ABC study enrolment activities. ABC: Ambiente e Biomonitoraggio nell'area di Civitavecchia, Environment and Biomonitoring in Civitavecchia.

Table 1
ABC study selected metals and their possible sources according to literature data, in particular the study National Health and Nutrition Examination Survey (NHANES)

	NHANES - USA	Other literature
Antimony (Sb)	Coal combustion	Diet; drinking water
Arsenic (As)		Coal plant; harbor; diet; drinking water
Berillium (Be)	Coal combustion; smoking	Smoking; diet; drinking water; hazardous waste
Cadmium (Cd)	Coal combustion; smoking	Coal plant; harbor; smoking
Cobalt (Co)	Coal and oil combustion; traffic	Dietary supplements
Chrome (Cr)		Coal plant; harbor; traffic; galvanic industry; smoking; diet
Cupper (Cu)		Coal plant, harbor; traffic
Iridium (Ir)		Traffic
Lead (Pb)	Coal combustion	Harbor; diet; drinking water
Manganese (Mn)		Harbor; combustion; diet
Mercury (Hg)	Coal combustion; diet	Coal plant; diet
Molybdenum (Mo)		Coal plant; diet; drinking water
Nickel (Ni)		Coal combustion; harbor; traffic; smoking; diet; jewelry; detergents
Palladium (Pd)	Traffic	Traffic
Platinum (Pt)		Traffic
Rhodium (Rh)		Traffic
Tallium (Tl)	Coal combustion	Coal combustion
Tin (Sn)		Coal combustion; petroleum; consumption of canned foods
Tungsten (W)		Combustion; cement plant; drinking water
Vanadium (V)		Harbor; fossil fluels; diet
Zinc (Zn)		Combustion; traffic; diet

ABC: Ambiente e Biomonitoraggio nell'area di Civitavecchia, Environment and Biomonitoring in Civitavecchia.

The determination of metals was carried out in a sample of first morning urine, that are more concentrated and improve the detection capability, compared to the spot urine, which are affected by greater variability in the dilution levels; the results were normalized to the urinary creatinine. The collection was carried out by a suitable 100 ml container (Kartell, polyethylene) decontaminated beforehand by washing with a 10% solution of HNO3 of ultrapure grade, to prevent possible metals contamination. Lead was instead determined in the blood, after collection in Vacutainer metal free tubes, specific for the analysis of trace elements.

Metals determination was performed by sector field inductively coupled plasma mass spectrometry with source (SF-ICP-MS). The instrument has been used in low, medium and high resolution in order to remove the spectral interference on the analyte signal. The method of standard additions in the matrix and the internal standardization were used to correct for any instrumental drifts and matrix effects. The method was validated by calculating the following parameters: repeatability intra-laboratory reproducibility, accuracy, measurement uncertainty, limit of detection/quantification, specificity, sensitivity, linearity, inter-laboratory proficiency tests. The method "Determination of the elements in biological matrices" (internal method, MI-05) has been accredited with UNI CEI EN ISO / IEC 17025. In cases where the values of the parameters were below the detection limit of the instrument (LOD), these have been replaced with a value equal to half LOD (LOD/2). Since certain metals in urine are affected by a further variability due to the different urinary density, the obtained measurements were corrected for the urinary creatinine to take account of the different urinary electrolytes concentrations. Geometric means and 95% Confidence Intervals of the metal concentrations, corrected for urinary creatinine, were calculated.

Medical visits and interviews

Each ABC participants underwent two medical visits. In the first visit, the participant received information about the objectives of the study, the organizing structures, ethical aspects and respect for the privacy rules and signed the declaration of consent to participate at the ABC study. A medical examination was subsequently performed during which the following measurements were performed: tests of lung function, saturometry (oxygen rate in the blood with an illuminated sensor placed on the fingertip), anthropometric (weight and height) and blood pressure measurements.

Various analytical and biological factors may affect the results of a biomonitoring study. Crucial factors to be considered are related to the exposure pathway, the presence of different sources of environmental pollution (including urban traffic and civil heating), physiological variables and lifestyles. Personal characteristics such as sex, age, weight and height can influence the metals concentration in the human body. Similarly certain diseases, although still subclinical level, the use of drug therapies, the presence of metal implants and dental amalgams, alcohol consumption, smoking, physical activity, diet (including local food consumption), the consumption of fish, milk and dairy products, the use of hormonal supplements, minerals and contraceptive drugs, the use of jewelry, the presence of piercing and tattoos, occupational exposure, are all factors capable of altering the amount of metals in the organism. Information on all of these potentially confounding factors were collected through a validate questionnaire administered by face to face interview.

At the end of the visit (first round) each participant was given a container to collect the urine in the morning, a diary to collect recent activities information and a bag for collecting nails (hands or feet) and hair (a strand diameter of about 1 cm in the rear corner area of the head), to be delivered to the second round. In the second round, in the next week (in the morning from 7.30 to 9.30) blood sampling, and urine, nails and hair collection was carried out.

Biological samples

The blood and urine collected in the course of the second visit were partly transported to the Civitavecchia hospital where blood-specific chemical tests (blood count, blood glucose, glycosylated hemoglobin, bilirubin, GOT, GPT, GGT, total cholesterol, HDL cholesterol, triglycerides, creatinine, uric acid, FT4, TSH) were carried out. The remaining samples were stored at -20 °C and periodically transferred to the Unit Bioelements and Health of the National Institute of Health (ISS) for the determination of metals (in urine: Sb, Be, Mo, Cd, Sn, W, Ir, Pt, Hg, Tl, V, Cr, Mn, Co, Ni, Cu, Zn, Rh, Pd, and As; in blood: Pb). Samples of urine and blood, together with a sample of nails and hair were preserved for possible future determinations at the Bioteca Foundation of Sarroch.

All the ABC participants received the results of blood and urine tests, the individual cardiovascular risk score, anthropometric measures, and respiratory function test results.

RESULTS

Characteristics of the ABC participants

Table 2 shows the main characteristics of the ABC sample (1177 participants) divided among the residents in the municipality of Civitavecchia (80%) and residents in the other municipalities of the district (20%). Females were 58% of the sample; about 60% aged between 45 and 64 years with a secondary or graduate school degree. No differences were found according to the municipality of residence. The prevalence of smoking in the ABC sample (25%) was higher among residents in the municipality of Civitavecchia (26%) compared to the other municipalities (21%), however no observed differences in the prevalence of smoking cessation (ex-smokers 36% in the total sample). Alcohol consumption was estimated in terms of assumed alcoholic units, based on the amount of wine, spirits and beer drinks; 25% of the subjects declared a habit of alcohol consumption by at least 2 glasses a day and this proportion reaches 27% among residents in other municipalities in the district. Relating to the Body Mass Index (BMI, calculated as the ratio of weight in kilograms and the square of height in meters) 42.4% of the

Table 2
Characteristics of ABC participants

		Civitavecchia 828		Other municipalities 349		Total 1177	
		n	%	n	%	n	%
Gender	Male	345	41.7	153	43.8	498	42.3
	Female	483	58.3	196	56.2	679	57.7
Age class	35-44	212	25.6	79	22.6	291	24.7
	45-54	241	29.1	113	32.4	354	30.1
	55-64	245	29.6	107	30.7	352	29.9
	≥ 65	129	15.6	51	14.6	180	15.3
Education	None/Primary	71	8.6	37	10.6	108	9.2
	Lower secondary school	245	29.6	117	33.5	362	30.8
	Upper secondary school	434	52.4	160	45.8	594	50.5
	Graduate/higher qualification	77	9.3	36	10.3	113	9.6
Occupation	Worker	437	52.8	190	54.4	627	53.3
	Unemployed	43	5.2	17	4.9	60	5.1
	Housewife	166	20.0	83	23.8	249	21.2
	Retired/Invalid	181	21.9	60	17.2	241	20.5
Smoking status	yes	217	26.2	74	21.2	291	24.7
	no	311	37.6	152	43.6	463	39.3
	ex	299	36.1	124	35.5	423	35.9
Alcohol	Never	233	28.1	102	29.2	335	28.5
	Less than one unit per week	157	19.0	53	15.2	210	17.8
	1-2 unit per week	166	20.0	66	18.9	232	19.7
	More than 2 unit per week	72	8.7	31	8.9	103	8.8
	1-2 unit per day	176	21.3	82	23.5	258	21.9
	More than 2 unit per day	23	2.8	16	4.6	39	3.3
Body Mass Index	Underweight (< 18.49)	8	1.0	2	0.6	10	0.8
	Normal weight (18.5-24.99)	264	31.9	115	33.0	379	32.2
	Overweight (25-29.99)	339	40.9	160	45.8	499	42.4
	Obese (30-34.99)	156	18.8	49	14.0	205	17.4
	Severely obese (> 34)	60	7.2	24	6.9	84	7.1
Occupation at risk*		246	29.7	58	16.6	304	25.8
Dental fillings	Amalgam	162	19.6	78	22.3	240	20.4
	All metals	211	25.5	96	27.5	307	26.1
Dentures metal		89	10.7	51	14.6	140	11.9
Metal fragments in the body**		291	35.1	140	40.1	431	36.6
Regular use of costume jewelry		413	49.9	160	45.8	573	48.7
Use of piercing		25	3.0	4	1.1	29	2.5
Tatoos on the body		116	14.0	33	9.5	149	12.7
Use of incense to perfume the house		31	3.7	12	3.4	43	3.7
Consumption of local foods		716	86.5	325	93.1	1041	88.4

*Initial smelting foundries; foundries second fusion; galvanic cell; welding, brazing, cutting and welding; production of plastic articles; the rubber industry; production paint; thermal power plant; cement; port; ships.
**Bearer of shrapnel or metal fragments, ferromagnetic clips, metallic intrauterine devices (spiral), metal implants, nails, screws.
ABC: Ambiente e Biomonitoraggio nell'area di Civitavecchia, Environment and Biomonitoring in Civitavecchia.

Table 3
Geometric means and 95% Confidence Intervals of the metal concentrations (corrected for urinary creatinine) among residents in the two areas of the district (town of Civitavecchia and other towns)

	Civitavecchia	Other municipalities	Total ABC Population
Antimony (Sb) µg/l	0.06	0.06	0.06
	0.05-0.06	0.05-0.07	0.05-0.06
Arsenic (As) µg/l	20.30	17.34	19.36
	18.54-22.22	15.34-19.60	17.98-20.83
Beryllium (Be) µg/l	0.12	0.13	0.13
	0.11-0.16	0.11-0.17	0.11-0.19
Cadmium (Cd) µg/l	0.42	0.43	0.42
	0.39-0.43	0.40-0.45	0.40-0.44
Cobalt (Co) µg/l	0.23	0.23	0.23
	0.21-0.24	0.21-0.25	0.21-0.24
Chromium (Cr) µg/l	0.13	0.13	0.13
	0.12-0.14	0.12-0.14	0.12-0.14
Iridium (Ir) ng/l	0.87	0.89	0.88
	0.83-0.95	0.83-0.91	0.85-0.91
Mercury (Hg) µg/l	1.23	1.05	1.17
	1.17-1.29	0.98-1.12	1.13-1.22
Manganese (Mn) µg/l	0.11	0.12	0.11
	0.09-0.11	0.10-0.13	0.10-0.11
Molybdenum (Mo) µg/l	38.23	38.59	38.34
	36.24-40.33	35.58-41.86	36.67-40.09
Nichel (Ni) µg/l	0.79	0.84	0.81
	0.75-0.84	0.77-0.91	0.77-0.85
Palladium (Pd) µg/l	15.99	16.10	16.02
	15.1-16.8	14.8-17.4	15.3-16.7
Lead in blood (Pb) ng/l	19.67	21.49	20.19
	19.02-20.34	20.35-22.69	19.62-20.78
Platinum (Pt) ng/l	2.65	2.40	2.57
	2.49-2.81	2.20-2.59	2.44-2.69
Copper (Cu) µg/l	6.95	7.29	7.05
	6.75-7.16	6.96-7.63	6.88-7.23
Rhodium (Rh) ng/l	17.03	15.81	16.65
	16.13-17.97	14.54-17.18	15.91-17.42
Tin (Sn) µg/l	0.32	0.31	0.32
	0.30-0.34	0.28-0.33	0.30-0.33
Thallium (Tl) µg/l	0.35	0.56	0.40
	0.33-0.37	0.50-0.63	0.38-0.42
Tungsten (W) µg/l	0.13	0.15	0.14
	0.12-0.14	0.13-0.17	0.13-0.15
Vanadium (V) µg/l	0.04	0.04	0.04
	0.03-0.04	0.03-0.04	0.04-0.04
Zinc (Zn) µg/l	286.58	275.62	283.22
	274.73-298.94	258.10-294.34	273.35-293.46

ABC: Ambiente e Biomonitoraggio nell'area di Civitavecchia, Environment and Biomonitoring in Civitavecchia.

ABC sample had a BMI above 25 – value defined by the WHO as a cut-off point for overweight – while in residents of other municipalities it reached the proportion of 45%; obese people was 17.4% (among residents in the municipality of Civitavecchia, this proportion was 19%) and 3.3% was severely obese (4.6 among residents in other municipalities). 25.8% of the sample had an occupation a priori defined as at risk (initial smelting foundries, secondary smelting foundries; galvanic cell, welding, brazing, cutting and welding; manufacture of plastic articles, rubber industry, paint production, thermoelectric plant; cement; harbor; ships), this proportion was 29% among residents in the town of Civitavecchia and 16.6% among those residing in other municipalities in the district. Information regarding metal implants, nails, wire, metal clips after surgery, metal fragments or metallic intrauterine devices were also obtained from the questionnaire. The use of intrauterine spiral may explains the high prevalence of people who reported being carriers of metals fragments in the body, however, it should be specified that while in the past intrauterine spirals were all in copper, those of the latest generation are constituted by a plastic holder that releases hormones. The interviews conducted showed that about 90% of the ABC sample habitually consumes foods produced locally.

Urinary concentrations of metals

Table 3 shows the geometric means of the metal concentrations (corrected for urinary creatinine) among residents in the two areas of the district (town of Civitavecchia and other towns).

No particular differences in metal concentrations based on the municipality of residence were observed. For arsenic, mercury, lead, and tungsten some differences between the two geographical areas were observed, probably due to different diet, lifestyle (*e.g.*, alcohol consumption, smoking, use of jewelry and piercings, tattoos, physical activity, hormonal and mineral supplements, and drugs), and occupational exposure.

CONCLUSIONS

The undergoing study on the association between biomarkers concentration and pollutants concentrations – estimated using a dispersion modeling approach, and adjusting for personal characteristics and concomitant other environmental exposure – could clarify the individual exposure of the residents in this industrial area.

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Conflict of interest statement

The authors declare that they have no conflicts of interest.

Components of the ABC Study Group

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