The Mario Negri Institute’s analytical capacities have enabled it to identify the 3,4,7,8-tetrachlorodibenzodioxin as the toxic outcome of the Seveso event in 1976. Monitoring the area at the time allowed the rapid transfer of people to uncontaminated areas. (Adamoli P et al. Analysis of 2,3,7,8-tetrachlorodibenzo-para-dioxin in the Seveso area. Ecological Bulletin 1978; 27: 31-38)

Treatment with progestogens does not protect pregnant women from spontaneous abortion. (Tognoni G et al. Progestagens in threatened abortion. Lancet 1980; 2: 1242-1243)

The Mario Negri Institute was one of the founders and supporters of clinical pharmacology. Over the years at the Institute a number of researchers from around the world have been formed in the discipline, and contributed to its implementation and development to a more appropriate use of drugs. (Bonati M, et al. Has clinical pharmacology lost its way? Lancet 1984; 1 : 556-558)

The GISSI studies have shown for the first time that a fibrinolytic agent can prevent mortality in 20% of patients with acute myocardial infarction (50% if treatment starts within three hours from infarction). (GISSI et al. Long-term effects of intravenous thrombolysis in acute myocardial infarction: Final report of the GISSI study. Lancet 1987; 2: 871-874)

Further studies have shown protective effect of nitrates, ACE inhibitors and aspirin on myocardial infarction. (ISIS-2, et al. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. Lancet 1988; 2: 349-360)


Therapeutic formularies, essential drugs, drug utilization studies characterized much of the activity of the Institute in the knowledge that this is a need for developing and a challenge for the developed countries. (Tognoni G, et al. Therapeutic formularies, essential drugs, drug utilization studies. WHO Reg Publ Eur Ser 1993 ; 45 : 43-53)

Intensive rather than traditional monitoring of patients with mammary cancer after surgery does not influence their survival. (GIVIO, Impact of follow-up testing on survival and health-related quality of life in breast cancer patients. A multicenter randomized controlled trial. JAMA 1994; 271: 1587-1592)

The Mario Negri Institute has largely contributed in its many years to the development of pharmacokinetics, introducing new analytical techniques such as gas and liquid chromatography combined or not with mass spectrometry. (Sottani C, et al. Structural characterization of mono- and dihydroxylated metabolites of paclitaxel in rat bile using liquid chromatography/ion spray tandem mass spectrometry. Rapid Commun Mass Spectrom 1997; 11: 1025-1032)


Valsartan significantly reduces the combined end point of mortality and morbidity and improves clinical signs and symptoms in patients with heart failure, when added to prescribed therapy. However, the post hoc observation of an adverse effect on mortality and morbidity in the subgroup receiving valsartan, an ACE inhibitor, and a beta-blocker raises concern about the potential safety of this specific combination. (Cohn J N, et al. A randomized trial of the angiotensin-receptor blocker Valsartan in chronic heart failure. N Engl J Med 2001; 345: 1667-1675)

Special attention was given to activities involving countries in the south of the world both training people from limited resources countries and setting up initiatives aimed at developing greater equity and appropriateness of care in needy countries. (Pandolfiši C, et al. Regulatory assessment of new drugs in developing countries. Lancet 2003 ; 362 : 249-250)

A technology has been developed to measure in slurry and water the amount of drugs of abuse consumed in a given area. Consumption patterns can therefore be followed during days and even years, and new drugs of abuse can be detected. This offers also a simple means of assessing the effect of campaigns to reduce the use of recreational drugs.


Ingredients of food that help protect against various tumors have been characterized. (Rossi M, et al. Flavonoids and the risk of oral and pharyngeal cancer: A case-control study from Italy. Cancer Epidemiol Biomarkers Prev 2007; 16: 1621-1625)


Old people’s kidneys can be used for transplantation (one or both) in old people with renal failure. (Rigotti P, et al. Outcome of renal transplantation from very old donors. N Engl J Med 2009; 360: 1464-1465)

Oligomers of β-amyloid are toxic in vitro and reduce memory in animals, showing that the neuronal toxicity of β-amyloid is not related solely to the presence of plaques. On this basis several drugs have proved able to antagonize the toxicity of β-amyloid oligomers with different mechanisms. (Balducci C, et al. Synthetic amyloid-beta-oligomers impair long-term memory independently of cellular prion protein. Proc Natl Acad Sci USA 2010; 107: 2295-2300)

Trabectedine, a drug derived from marine organisms, essentially developed at “Mario Negri” labs, is active in some types of ovarian cancer and soft sarcomas. (for example Germano G, et al. Antitumor and anti-inflammatory effects of trabectedin on human mixoid liposarcoma cells. Cancer Res 2010; 70: 2235-2244)

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The malignancy of ovarian cancer can be predicted from the level of miRNA 200c with an inverse relationship. This allows to determine the intensity of the chemotherapy. (Marchini S, et al. Association between miR-200c and the survival of patients with stage I epithelial ovarian cancer: a retrospective study of two independent tumour tissue collections. Lancet Oncol 2011; 12: 273-285)


Experimental studies on stroke show activation of the complement cascade as well as an increase of the mannose binding protein (MBP). Effective drugs have been developed. (Frigerio F, et al. Long-lasting pro-ictogenic effects induced in vivo by rat brain exposure to serum albumin in the absence of concomitant pathology. Epilepsia 2012; 53: 1887-1897)

Various epidemiological studies have contributed to the quantification of the excess risk of cancer in relation to type 2 diabetes mellitus (Bosetti C, et al. Diabetes mellitus and cancer risk in a network of case-control studies. Nutr Cancer 2012; 64: 643-651)

A RCT on non-small cell lung cancer found that erlotinib, an expensive drug, is inferior to the generic drug docetaxel. (Garassino M C, et al. Erlotinib versus docetaxel as second-line treatment of patients with advanced non-small-cell lung cancer and wild-type EGFR tumours (TAILOR): a randomised controlled trial. Lancet Oncol 2013; 14: 981-988)

Pharmacokinetic studies have shown that anticancer agents are not distributed uniformly in tumors because they fail to reach several areas at the center of the tumor. This shows that certain cancer cells that proliferate seem to be resistant but in fact they have not come into contact with the drug. (Morosi L, et al. Determination of paclitaxel distribution in solid tumors by nano-particle assisted laser desorption ionization mass spectrometry imaging. PLoS One 2013; 8: e72532)

The Mario Negri Institute has made available “Intercheck”, a platform concerning the potential interactions between drugs and between drugs and food or herbal extracts. (Ghibelli S, et al. Prevention of inappropriate prescribing in hospitalized older patients using a computerized prescription support system (INTERcheck ®). Drugs Aging 2013; 30: 821-828)

A large RCT involving about 800 Italian practitioners showed no benefit of omega-3 fatty acids on cardiovascular mortality. These products were included in the list of drugs reimbursed by the NHS. (Risk and Prevention Study Collaborative Group et al. n3 Fatty acids in patients with multiple cardiovascular risk factors. N Engl J Med 2013; 368: 1800-1808)


We showed that women treated with trastuzumab-based adjuvant regimen for HER2-positive early breast cancer in clinical practice, have a survival rate within the fourth year of follow-up (89.4%) consistent with estimates from clinical trials. Regimens lasting < 6 months resulted in a worse prognosis (Bonifazi M, et al. Long term survival of HER2-positive early breast cancer treated with trastuzumab-based adjuvant regimen: a large cohort study from clinical practice. Breast 2014; 23: 573-578)


To ensure a better mother, child, and adolescent well-being by undertaking interdisciplinary and collaborative work in the field was one of the activities of the Institute, also involving countries of the north and south of the world. Networks of physicians (obstetric-gynecologists, neonatologists, pediatricians, and child psychiatrists) and of parents were set up, and maintained in the years. One of the main achievements was the first ever performed RCT involving family pediatricians as investigators, the results of which showed the scant effectiveness of inhaled steroids in preventing viral wheezing: a wide improper practice in Italian children. (Clavenna A, et al. Effectiveness of nebulized beclometasone in preventing viral wheezing: an RCT. Pediatrics 2014 ; 133 : e505-e512)

Through Italian and European cross-sectional studies we have shown that the increase in tobacco taxation is the main strategy for tobacco control. (Gallus S, et al Pricing Policies And Control of Tobacco in Europe (PPACTE) project: cross-national comparison of smoking prevalence in 18. European countries. Eur J Cancer Prev 2014; 23: 177-185).


Definition of the genetic structure and function of molybdoflavoproteins (aldehyde oxidases and xanthine oxidoreductase), a family of enzymes involved in the catabolism of purines and in drug metabolism. (Terao M, et al. Structure and function of mammalian aldehyde oxidases. Arch Toxicol 2016; 90: 753-780)

Comparative studies on schizophrenic patients show that a new agent, aripiprazole, is no better than olanzepine and haloperidol. (Parabiaghi A, et al. Metabolic syndrome and drug discontinuation in schizophrenia: a randomized trial comparing aripiprazole olanzapine and haloperidol. Acta Psychiatr Scand 2016; 133: 63-75)

Comparative studies on analgesic agents do not show any differences between morphine, buprenorphine, oxycodone and fentanyl in terms of efficacy but there are differences in resistance and adverse reactions. (Corli O, et al. Are strong opioids equally effective and safe in the treatment of chronic cancer pain? A multicenter randomized phase 4 ‘real life’ trial on the variability of response to opioids. Ann Oncol 2016; E-pub)


Specific neuroinflammatory pathways in epilepsies have led to the development of new anticonvulsant agents. (Iori V, et al. miR-146a-based therapy against neuroinflammation has anti-ictogenetic and disease-modifying effects in murine of seizures and epilepsy. (submitted)

The Mario Negri Institute has significantly contributed to the creation of the Italian National Health Service (NHS) (1978), to promoting laws against smoking, to revision of the Formulary of drugs reimbursed by the NHS and to establishing the European law on orphan drugs.

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SG/vp